



ADVANCED LABORATORY TESTING METHODS IN GASTROENTEROLOGY NURSING FOR EARLY DETECTION OF DRUG-INDUCED LIVER INJURY

Zainab abdullah alhuzaym^{1*}, Mukhtar muslim h bujubarah², Ahmed naser alzaher³, Al Rashed, Ahmed Gaafar A⁴, Alamri, aljuri Ali m⁵, Hanan Ahmed Mohammed Alzahrani⁶, Salhah Ali Alshihri⁷, Abdullah Ali Alamer⁸, Zahra yousef alnajadi⁹, Almuqadam, Jamilah Salem H¹⁰, Alasiri saleh Abdulrahman¹¹, Ali Fayi Alabdali¹², Assiri, Ibrahim Ali H¹³, Tariq meshal alshammari¹⁴, Mohammed meshal Farhan¹⁵

^{1*}Nurse technician, Maternity and children hospital, Alahsa, Saudi Arabia.

²Nursing specialist, Eradah Complex For Mental Health Dammam, Saudi Arabia.

³Lab technician, Safwa General Hospital, Saudi Arabia.

⁴Laboratory specialist, Maternity and children hospital, Alahsa, Saudi Arabia.

⁵Nurse, Taybah aljanubiah health center, Saudi Arabia.

⁶Nurse technician, Althager hospital, Saudi Arabia.

⁷Nurse specialist, Alaziziyah Children Hospital, Jeddah, Saudi Arabia.

⁸Nurse technician -operation room, Maternity and children hospital, Alahsa, Saudi Arabia.

⁹Nurse, King fahad hospital hofuf, Saudi Arabia.

¹⁰Nursing, Alaziziah children hospital, Saudi Arabia.

¹¹Pharmacist, KFMC Southern region, Saudi Arabia.

¹²Pharmacy technician, Rejal Almaa Health Sector, Saudi Arabia.

¹³Prince Faisal Bin Khaled Cardiac center, Abha, Saudi Arabia.

¹⁴Pharmacist technician, Maternity and children hospital Hail, Saudi Arabia.

¹⁵Pharmacy, king khalid hospital, MOH, Hail, Saudi Arabia.

***Corresponding Author:** Zainab abdullah alhuzaym

*Nurse technician, Maternity and children hospital, Alahsa, Saudi Arabia.

Abstract:

Drug-induced liver injury is a significant concern in clinical practice, as it can lead to severe complications if not detected and managed promptly. Gastroenterology nurses play a crucial role in monitoring patients for signs of DILI and implementing appropriate interventions to prevent further liver damage. By utilizing advanced laboratory testing methods, such as biomarker analysis, genetic testing, and imaging techniques, nurses can enhance their ability to identify DILI at an early stage, allowing for timely intervention and improved patient outcomes. This review discusses the current landscape of laboratory testing methods in gastroenterology nursing, their applications in detecting DILI, and the challenges and opportunities associated with their implementation in clinical practice. Furthermore, it highlights the importance of ongoing education and training for nurses to stay abreast of the latest advancements in laboratory testing for DILI detection.

Keywords: Drug-induced liver injury, Gastroenterology nursing, Advanced laboratory testing methods, Biomarker analysis, Genetic testing, Early detection

Introduction:

Drug-induced liver injury (DILI) is a serious and potentially life-threatening condition that can result from the use of various medications. It is important for healthcare providers, including gastroenterology nurses, to be able to detect DILI early in order to prevent further liver damage and provide appropriate treatment. Advanced laboratory testing methods play a crucial role in the early detection of DILI, allowing healthcare providers to identify patients at risk and take necessary precautions [1].

Gastroenterology nurses are often on the front lines of patient care, working closely with individuals who are taking medications that may pose a risk of DILI. These nurses play a key role in monitoring patients for signs and symptoms of liver injury and in coordinating care with other members of the healthcare team. Advanced laboratory testing methods provide an important tool for gastroenterology nurses in the early detection of DILI [2].

One of the most commonly used laboratory tests for the detection of DILI is liver function tests (LFTs). These tests measure levels of various enzymes and proteins in the blood that are released by the liver when it is damaged. Elevations in these levels can indicate liver injury and prompt further evaluation. Gastroenterology nurses are often responsible for ordering and interpreting LFTs and communicating the results to other members of the healthcare team [3].

In addition to LFTs, other advanced laboratory testing methods can also be used in the early detection of DILI. For example, tests for specific biomarkers of liver injury, such as glutathione S-transferase alpha (GST- α) and microRNA-122, can provide more sensitive and specific information about the extent of liver damage. These tests can help healthcare providers to differentiate between different types of liver injury and to determine the most appropriate course of treatment [4].

Another advanced laboratory testing method that is increasingly being used in the early detection of DILI is genetic testing. Certain genetic variations can increase an individual's risk of developing DILI in response to specific medications. By identifying these genetic markers, healthcare providers can tailor treatment plans to reduce the risk of liver injury in susceptible individuals. Gastroenterology nurses play a critical role in collecting and interpreting genetic test results and in educating patients about their implications [5].

Role of Gastroenterology Nurses in DILI Detection and Management:

Gastroenterology nurses play a crucial role in the detection and management of drug-induced liver injury (DILI). DILI is a serious and potentially life-threatening condition that occurs as a result of exposure to certain medications, herbal remedies, or dietary supplements. It is important for healthcare providers, including gastroenterology nurses, to be vigilant in identifying and managing DILI in order to prevent further liver damage and complications [6].

One of the key roles of gastroenterology nurses in DILI detection is to monitor patients for signs and symptoms of liver injury. This includes conducting thorough assessments of patients' medical histories, medications, and symptoms, as well as performing physical exams and ordering diagnostic tests such as liver function tests and imaging studies. Gastroenterology nurses must be knowledgeable about the various medications and substances that can cause DILI, as well as the risk factors and warning signs associated with this condition [7].

In addition to monitoring patients for signs of DILI, gastroenterology nurses also play a critical role in educating patients about the importance of medication safety and adherence. This includes providing patients with information about the potential risks and side effects of their medications, as well as counseling them on how to properly take their medications and avoid harmful interactions with other substances. Gastroenterology nurses may also work closely with other healthcare providers to develop individualized care plans for patients at risk for DILI, including monitoring their liver function regularly and adjusting their medications as needed [8].

When DILI is suspected or diagnosed, gastroenterology nurses are instrumental in managing the condition and coordinating care for patients. This may involve providing supportive care to help patients recover from liver injury, monitoring their progress closely, and collaborating with other members of the healthcare team to determine the best course of treatment. Gastroenterology nurses

may also play a role in advocating for patients and ensuring that they receive appropriate follow-up care and monitoring to prevent further liver damage [9].

Overall, gastroenterology nurses play a vital role in the detection and management of DILI. Their expertise in assessing patients, educating them about medication safety, and coordinating care makes them invaluable members of the healthcare team. By working collaboratively with other healthcare providers and advocating for patients, gastroenterology nurses can help to improve outcomes for patients with DILI and ensure that they receive the care and support they need to recover from this potentially serious condition [10].

Overview of Advanced Laboratory Testing Methods in Gastroenterology Nursing:

Gastroenterology nursing is a specialized field that focuses on the care and treatment of patients with disorders of the digestive system. Advanced laboratory testing methods play a crucial role in the diagnosis and management of these conditions [11].

One of the most commonly used advanced laboratory testing methods in gastroenterology nursing is endoscopy. Endoscopy is a minimally invasive procedure that allows healthcare providers to visualize the inside of the digestive tract using a thin, flexible tube with a camera attached to it. This procedure can help diagnose a wide range of gastrointestinal conditions, including ulcers, polyps, and cancer. Endoscopy can also be used to take tissue samples for biopsy, which can help healthcare providers determine the cause of certain gastrointestinal symptoms [12].

Another important advanced laboratory testing method in gastroenterology nursing is fecal occult blood testing. This test is used to detect the presence of blood in the stool, which can be a sign of gastrointestinal bleeding. Fecal occult blood testing is often used as a screening tool for colorectal cancer, as well as other gastrointestinal conditions such as ulcers and inflammatory bowel disease. This test is simple, non-invasive, and can be done at home with a test kit [13].

Genetic testing is another advanced laboratory testing method that is becoming increasingly important in gastroenterology nursing. Genetic testing can help healthcare providers determine a patient's risk for developing certain gastrointestinal conditions, such as hereditary colon cancer syndromes. This information can help guide treatment decisions and screening recommendations for patients with a family history of gastrointestinal disorders. Genetic testing can also help healthcare providers personalize treatment plans for patients with certain genetic mutations that may affect their response to medications [14].

In addition to these advanced laboratory testing methods, there are a number of other tests that are commonly used in gastroenterology nursing, including imaging studies such as CT scans, MRIs, and ultrasound. These tests can help healthcare providers visualize the structure and function of the digestive tract, and can be used to diagnose a wide range of gastrointestinal conditions. Blood tests are also commonly used in gastroenterology nursing to assess liver function, check for signs of inflammation or infection, and monitor the effectiveness of treatment [15].

Advanced laboratory testing methods play a crucial role in the diagnosis and management of gastrointestinal conditions in gastroenterology nursing. Endoscopy, fecal occult blood testing, genetic testing, and imaging studies are just a few of the advanced laboratory testing methods that are commonly used in this field. These tests can help healthcare providers diagnose gastrointestinal disorders, monitor treatment effectiveness, and personalize treatment plans for patients. As technology continues to advance, it is likely that new and innovative laboratory testing methods will continue to emerge in gastroenterology nursing, further improving patient care and outcomes [16].

Importance of Biomarker Analysis in Early Detection of DILI:

Drug-induced liver injury (DILI) is a serious and potentially life-threatening condition that occurs when a medication or other substance damages the liver. It is a major concern for healthcare providers and patients alike, as DILI can lead to liver failure, the need for a liver transplant, or even death. Early detection of DILI is crucial in order to prevent these serious consequences, and one important tool in the early detection of DILI is biomarker analysis [17].

Biomarkers are measurable substances or indicators that can be used to assess the presence or severity of a disease or condition. In the case of DILI, biomarkers can provide valuable information about the health of the liver and help to identify patients who may be at risk for developing DILI. Biomarker analysis can also help to monitor the progression of DILI and assess the effectiveness of treatment [18].

There are several different types of biomarkers that can be used in the early detection of DILI. Liver enzymes, such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST), are commonly used biomarkers for liver damage. Elevated levels of these enzymes in the blood can indicate that the liver is being damaged and may be a sign of DILI. Other biomarkers, such as bilirubin and alkaline phosphatase, can also provide important information about the health of the liver [19].

In addition to measuring liver enzymes and other traditional biomarkers, newer biomarkers are being developed that may provide even more specific and sensitive information about DILI. For example, microRNAs are small molecules that can be used as biomarkers for liver damage. These molecules are released into the blood when the liver is injured, and measuring their levels can provide valuable information about the extent of liver damage and the risk of developing DILI [20].

Biomarker analysis is particularly important in the early detection of DILI because the symptoms of DILI can be nonspecific and may be mistaken for other conditions. For example, symptoms of DILI can include fatigue, nausea, and abdominal pain, which are also common symptoms of many other conditions. By using biomarker analysis to assess the health of the liver, healthcare providers can more accurately diagnose DILI and begin treatment sooner [21].

Early detection of DILI is crucial in order to prevent serious complications and improve patient outcomes. If DILI is detected early, treatment can be initiated promptly to prevent further liver damage and improve the chances of recovery. Biomarker analysis plays a key role in the early detection of DILI by providing valuable information about the health of the liver and helping to identify patients who may be at risk for developing DILI [22].

Biomarker analysis is an important tool in the early detection of DILI. By measuring biomarkers such as liver enzymes and microRNAs, healthcare providers can assess the health of the liver, monitor the progression of DILI, and determine the effectiveness of treatment. Early detection of DILI is crucial in order to prevent serious complications and improve patient outcomes, and biomarker analysis plays a key role in achieving this goal. By using biomarker analysis in the early detection of DILI, healthcare providers can provide more accurate diagnoses, initiate treatment sooner, and ultimately improve patient outcomes [23].

Application of Genetic Testing in Identifying Susceptibility to DILI:

Drug-induced liver injury (DILI) is a serious adverse drug reaction that can result in liver dysfunction, failure, or even death. It is a major concern in clinical practice and drug development, as it can lead to the withdrawal of potentially beneficial medications from the market. Identifying patients who are at an increased risk of developing DILI is crucial for preventing this adverse event and improving patient safety. Genetic testing has emerged as a promising tool for identifying individuals who may be susceptible to DILI [24].

Genetic testing involves analyzing an individual's DNA to identify variations in genes that may influence their response to medications. These variations, known as genetic polymorphisms, can affect the way drugs are metabolized, transported, or interact with target proteins in the body. By identifying genetic markers associated with DILI susceptibility, healthcare providers can personalize treatment plans and monitor patients more closely to prevent adverse drug reactions [3].

Several genes have been implicated in DILI susceptibility, including those involved in drug metabolism, immune response, and liver function. For example, variations in genes encoding drug-metabolizing enzymes such as cytochrome P450 (CYP) enzymes can affect the rate at which drugs are broken down in the liver. Slow metabolizers may be at an increased risk of developing DILI due to higher drug concentrations in the body, while fast metabolizers may be at a lower risk [12].

In addition to drug metabolism genes, genetic variations in genes involved in immune response can also play a role in DILI susceptibility. The immune system plays a critical role in the pathogenesis of

DILI, as it can mount an inflammatory response against drug-induced liver damage. Genetic markers associated with immune response pathways can help identify individuals who may be predisposed to developing DILI due to an exaggerated immune reaction [26].

Furthermore, genetic testing can also identify individuals with underlying liver conditions that may increase their susceptibility to DILI. For example, variations in genes involved in liver function, such as those encoding transport proteins or antioxidant enzymes, can affect the liver's ability to detoxify drugs and protect against oxidative stress. Individuals with genetic mutations that impair liver function may be at a higher risk of developing DILI when exposed to certain medications [13].

The application of genetic testing in identifying susceptibility to DILI has the potential to revolutionize personalized medicine and improve patient outcomes. By integrating genetic information into clinical decision-making, healthcare providers can tailor treatment plans to individual patients based on their genetic risk factors. This personalized approach can help prevent adverse drug reactions, optimize drug efficacy, and minimize healthcare costs associated with DILI [9].

Despite the promising potential of genetic testing in DILI susceptibility, there are still challenges that need to be addressed. One of the main challenges is the interpretation of genetic data and the translation of research findings into clinical practice. Healthcare providers need to be educated on the utility of genetic testing in DILI susceptibility and how to integrate genetic information into patient care effectively [31].

Genetic testing is a valuable tool for identifying individuals who may be susceptible to DILI. By analyzing genetic markers associated with drug metabolism, immune response, and liver function, healthcare providers can personalize treatment plans and monitor patients more closely to prevent adverse drug reactions. The application of genetic testing in DILI susceptibility has the potential to revolutionize personalized medicine and improve patient safety in clinical practice [7].

Imaging Techniques for Assessing Liver Damage in DILI:

Drug-induced liver injury (DILI) is a serious and potentially life-threatening condition that occurs when the liver is damaged by the use of certain medications or toxins. It is a major concern in clinical practice, as it can lead to liver failure and even death if not detected and managed promptly. Imaging techniques play a crucial role in the assessment of liver damage in DILI, providing valuable information about the extent and severity of the injury [22].

There are several imaging techniques that can be used to assess liver damage in DILI, each with its own advantages and limitations. Some of the most commonly used imaging techniques include ultrasound, computed tomography (CT) scan, magnetic resonance imaging (MRI), and transient elastography [13].

Ultrasound is often the first imaging modality used to assess liver damage in DILI, as it is non-invasive, readily available, and relatively inexpensive. Ultrasound can provide information about the size, shape, and texture of the liver, as well as the presence of any abnormalities such as liver cysts or tumors. However, ultrasound has limited sensitivity and specificity for detecting early or mild liver damage, and may not be able to accurately assess the extent of liver injury in DILI [5].

CT scan is another commonly used imaging technique for assessing liver damage in DILI. CT scan can provide detailed images of the liver and surrounding structures, allowing for the detection of liver lesions, inflammation, and fibrosis. CT scan is particularly useful for evaluating the extent of liver damage in DILI and for monitoring changes in liver morphology over time. However, CT scan involves exposure to ionizing radiation, which may limit its use in certain patient populations, such as pregnant women or children [22].

MRI is a powerful imaging technique that can provide detailed images of the liver without the use of ionizing radiation. MRI can be used to assess liver damage in DILI by evaluating liver morphology, blood flow, and tissue composition. MRI is particularly useful for detecting early or mild liver damage, as well as for distinguishing between different types of liver lesions. However, MRI is more expensive and less readily available than ultrasound or CT scan, which may limit its use in some clinical settings [23].

Transient elastography is a specialized imaging technique that can be used to assess liver fibrosis in DILI. Transient elastography measures the stiffness of the liver tissue, which is an important indicator of liver damage and fibrosis. Transient elastography is non-invasive, quick, and easy to perform, making it a valuable tool for monitoring liver fibrosis in DILI. However, transient elastography has limited sensitivity for detecting early or mild liver damage, and may not be able to accurately assess the extent of liver injury in DILI [24].

Imaging techniques play a crucial role in the assessment of liver damage in DILI. Ultrasound, CT scan, MRI, and transient elastography are valuable tools for evaluating liver morphology, inflammation, fibrosis, and function in patients with DILI. Each imaging technique has its own advantages and limitations, and the choice of imaging modality should be based on the specific clinical scenario and the goals of the assessment. By using a combination of imaging techniques, clinicians can accurately assess liver damage in DILI and provide timely and appropriate management for affected patients [25].

Challenges and Opportunities in Implementing Advanced Laboratory Testing Methods in Clinical Practice:

In recent years, there has been a significant advancement in laboratory testing methods, which have revolutionized the field of clinical practice. These advanced testing methods offer more accurate and precise results, leading to better diagnosis and treatment of various medical conditions. However, implementing these advanced laboratory testing methods in clinical practice comes with its own set of challenges and opportunities [26].

Challenges in Implementing Advanced Laboratory Testing Methods

One of the major challenges in implementing advanced laboratory testing methods in clinical practice is the cost involved. These advanced testing methods often require expensive equipment and reagents, which can be a barrier for many healthcare facilities, especially in developing countries. Additionally, the training and expertise required to perform these tests accurately can also be a challenge, as not all healthcare professionals may be familiar with the new technologies [27].

Another challenge is the time-consuming nature of some advanced laboratory testing methods. Some tests may require longer processing times, which can delay the diagnosis and treatment of patients. This can be particularly problematic in emergency situations where quick results are crucial for patient care [28].

Furthermore, the complexity of some advanced laboratory testing methods can also be a challenge. Interpreting the results of these tests may require specialized knowledge and training, which may not be readily available in all healthcare settings. This can lead to misinterpretation of results and potentially incorrect diagnosis and treatment of patients [29].

Opportunities in Implementing Advanced Laboratory Testing Methods

Despite the challenges, there are also numerous opportunities in implementing advanced laboratory testing methods in clinical practice. One of the biggest opportunities is the potential for more accurate and precise diagnosis of medical conditions. Advanced testing methods can detect diseases at an earlier stage, leading to better outcomes for patients. Additionally, these tests can also help in monitoring the effectiveness of treatments and adjusting them as needed [30].

Another opportunity is the potential for personalized medicine. Advanced laboratory testing methods can provide more detailed information about a patient's genetic makeup, allowing for tailored treatment plans based on individual characteristics. This can lead to more effective and targeted therapies, minimizing the risk of adverse reactions and improving patient outcomes [31].

Furthermore, advanced laboratory testing methods can also improve the efficiency of healthcare systems. By providing quicker and more accurate results, these tests can help in streamlining the diagnostic process and reducing unnecessary tests and procedures. This can lead to cost savings for healthcare facilities and better allocation of resources [32].

Implementing advanced laboratory testing methods in clinical practice comes with its own set of challenges and opportunities. While the cost, complexity, and time-consuming nature of these tests

may pose obstacles, the potential for more accurate diagnosis, personalized medicine, and improved efficiency in healthcare systems make it a worthwhile endeavor. By addressing the challenges and leveraging the opportunities, healthcare facilities can harness the power of advanced laboratory testing methods to provide better care for their patients [33].

Conclusion:

In conclusion, advanced laboratory testing methods are essential tools in the early detection of DILI in patients taking medications that may pose a risk of liver injury. Gastroenterology nurses play a crucial role in implementing these testing methods, interpreting the results, and coordinating care with other members of the healthcare team. By using advanced laboratory testing methods effectively, gastroenterology nurses can help to ensure the early detection of DILI and the prompt initiation of appropriate treatment, ultimately improving patient outcomes and reducing the risk of serious liver damage.

References:

1. Fontana RJ, Watkins PB, Bonkovsky HL, et al. Drug-Induced Liver Injury Network (DILIN) prospective study: rationale, design and conduct. *Drug Saf.* 2009;32(1):55-68.
2. Björnsson ES. Drug-induced liver injury: an overview over the most critical compounds. *Arch Toxicol.* 2015;89(3):327-334.
3. Teschke R, Danan G. Diagnosis and management of drug-induced liver injury (DILI) in patients with pre-existing liver disease. *Drug Saf.* 2016;39(8):729-744.
4. Chalasani N, Fontana RJ, Bonkovsky HL, et al. Causes, clinical features, and outcomes from a prospective study of drug-induced liver injury in the United States. *Gastroenterology.* 2008;135(6):1924-1934.
5. Sgro C, Clinard F, Ouazir K, et al. Incidence of drug-induced hepatic injuries: a French population-based study. *Hepatology.* 2002;36(2):451-455.
6. Andrade RJ, Robles M, Fernández-Castañer A, López-Ortega S, López-Vega MC, Lucena MI. Assessment of drug-induced hepatotoxicity in clinical practice: a challenge for gastroenterologists. *World J Gastroenterol.* 2007;13(3):329-340.
7. Navarro VJ, Senior JR. Drug-related hepatotoxicity. *N Engl J Med.* 2006;354(7):731-739.
8. Reuben A, Koch DG, Lee WM; Acute Liver Failure Study Group. Drug-induced acute liver failure: results of a U.S. multicenter, prospective study. *Hepatology.* 2010;52(6):2065-2076.
9. Lee WM. Drug-induced hepatotoxicity. *N Engl J Med.* 2003;349(5):474-485.
10. Lewis JH. Drug-induced liver injury throughout the drug development life cycle: where we have been, where we are now, and where we are headed. *Drug Saf.* 2016;39(9):801-814.
11. Aithal GP, Watkins PB, Andrade RJ, et al. Case definition and phenotype standardization in drug-induced liver injury. *Clin Pharmacol Ther.* 2011;89(6):806-815.
12. Lucena MI, Andrade RJ, Kaplowitz N, et al. Phenotypic characterization of idiosyncratic drug-induced liver injury: the influence of age and sex. *Hepatology.* 2009;49(6):2001-2009.
13. Robles-Díaz M, Medina-Caliz I, Stephens C, et al. Drug-induced liver injury: a review. *Int J Mol Sci.* 2016;17(9):E141.
14. Danan G, Teschke R. RUCAM in drug and herb induced liver injury: the update. *Int J Mol Sci.* 2016;17(1):E14.
15. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of non-alcoholic fatty liver disease: practice guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association. *Hepatology.* 2012;55(6):2005-2023.
16. Björnsson ES. Hepatotoxicity by drugs: the most common implicated agents. *Int J Mol Sci.* 2016;17(2):E224.
17. Teschke R, Schwarzenboeck A, Hennermann KH. Causality assessment in hepatotoxicity by drugs and dietary supplements. *Br J Clin Pharmacol.* 2008;66(4):503-515.

18. Andrade RJ, Lucena MI, Fernández MC, Pelaez G, Pachkoria K, Garcia-Ruiz E, et al. Drug-induced liver injury: an analysis of 461 incidences submitted to the Spanish registry over a 10-year period. *Gastroenterology*. 2005;129(2):512-521.
19. Reuben A. Hy's law. *Hepatology*. 2004;39(2):574-578.
20. Teschke R, Eickhoff A, Schulze J. Drug induced liver injury: can biomarkers assist RUCAM in causality assessment? *Int J Mol Sci*. 2017;18(4):E803.
21. Andrade RJ, Aithal GP, Björnsson ES, et al. EASL Clinical Practice Guidelines: drug-induced liver injury. *J Hepatol*. 2019;70(6):1222-1261.
22. Kaplowitz N. Drug-induced liver injury. *Clin Infect Dis*. 2004;38(Suppl 2):S44-S48.
23. Björnsson ES, Hoofnagle JH. Categorization of drugs implicated in causing liver injury: critical assessment based on published case reports. *Hepatology*. 2016;63(2):590-603.
24. Teschke R, Wolff A, Frenzel C, Schulze J, Eickhoff A. Drug induced liver injury: accuracy of diagnosis in published reports. *Ann Hepatol*. 2014;13(2):248-255.
25. Chalasani N, Bonkovsky HL, Fontana R, et al. Features and outcomes of 899 patients with drug-induced liver injury: the DILIN prospective study. *Gastroenterology*. 2015;148(7):1340-1352.
26. Fontana RJ. Pathogenesis of idiosyncratic drug-induced liver injury and clinical perspectives. *Gastroenterology*. 2014;146(4):914-928.
27. Andrade RJ, Robles M, Ulzurrún E, Lucena MI. Drug-induced liver injury: insights from genetic studies. *Pharmacogenomics*. 2009;10(9):1467-1487.
28. Teschke R, Danan G. Drug induced liver injury with analysis of alternative causes as confounding variables. *Br J Clin Pharmacol*. 2018;84(7):1467-1477.
29. Aithal GP. Hepatotoxicity related to antirheumatic drugs. *Nat Rev Rheumatol*. 2011;7(3):139-150.
30. Björnsson ES, Bergmann OM, Björnsson HK, Kvaran RB, Olafsson S. Incidence, presentation, and outcomes in patients with drug-induced liver injury in the general population of Iceland. *Gastroenterology*. 2013;144(7):1419-1425.
31. Andrade RJ, Lucena MI, Kaplowitz N, et al. Outcome of acute idiosyncratic drug-induced liver injury: long-term follow-up in a hepatotoxicity registry. *Hepatology*. 2006;44(6):1581-1588.
32. Reuben A, Koch DG, Lee WM; Acute Liver Failure Study Group. Acute liver failure study group. Drug-induced acute liver failure: results of a U.S. multicenter, prospective study. *Hepatology*. 2010;52(6):2065-2076.
33. Lee WM. Acute liver failure. *Semin Respir Crit Care Med*. 2012;33(1):36-45.