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Advancements in Sensitivity Testing for Hepatitis C Screening: A Literature Review of Innovations, Challenges, and Clinical Effectiveness

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ABSTRACT
Early detection of HCV is crucial for initiating timely treatment and reducing transmission, particularly in high-risk populations. This review explores advancements in sensitivity testing for Hepatitis C virus (HCV), focusing on innovations, challenges, and clinical effectiveness. Nucleic Acid Testing (NAT) has significantly enhanced diagnostic capabilities by detecting HCV RNA much earlier than antibody-based tests, reducing the window period and improving patient outcomes. However, the high cost and technical complexity of NAT limit its widespread adoption, particularly in low and middle-income countries (LMICs). Rapid Diagnostic Tests (RDTs) offer a more accessible and cost-effective alternative in resource-limited settings, although they generally have lower sensitivity, especially in early-stage infections. Recent innovations in RDT technology, including dual-detection mechanisms for both antibodies and antigens, have improved their clinical utility but cannot fully replace NAT in accuracy. This review also addresses the variability in test performance across different populations influenced by factors such as age, immune status, and co-infection with other viruses like Human Immunodeficiency Virus (HIV). These factors create challenges in standardizing screening programs globally, as tests that perform well in one population may not be effective in another. The need for tailored diagnostic approaches that account for these variables is critical for ensuring accurate and early detection of HCV in diverse regions. While technological advancements have improved HCV diagnostics, challenges related to cost, accessibility, and test variability persist. Continuous innovation and investment in affordable and accessible diagnostic tools are necessary to expand global screening efforts, particularly in LMICs. Addressing these challenges is essential for achieving the World Health Organization's goal of eliminating HCV as a public health threat by 2030.

Keywords: Hepatitis C Virus (HCV), Nucleic Acid Testing (NAT),Rapid Diagnostic Tests (RDTs), HCV sensitivity testing, Diagnostic Innovations;;

1.0 INTRODUCTION

Millions of people are suffering with HCV worldwide. WHO estimated the prevalence of HCV infection as 58 millions of chronic HCV infections and 1.5 millions of new infections annually. The virus causes cirrhosis, liver failure, and hepatocellular carcinoma. The "silent epidemic" of hepatitis C rarely develops symptoms until it reached to anadvanced stage. Early detection helps to reduce the viruses infections and improve the patientrecovery process. HCV sensitivity testing has revolutionized HCV diagnosis and therapy, enabling early detection and treatment for the prevention of the diasease[1]. HCV screening sensitivity testing is able to detect the virus or its markers such as antibodies or viral RNA in infected patients at low levels or concentration making the diagnosis identifiable at early stage. Sensitivity testing advances have enhanced diagnostic accuracy, speed, and accessibility, reducing the infection-detectability window. The window period must be decreased to avoid HCV transmission, especially in high-risk populations including intravenous drug users and medical workers with poor infection control. Advanced diagnostics could modify HCV transmission and disease progression worldwide[2].

Early HCV screening methods used host immune reaction antibodies and were less sensitive. Years ago, HCV diagnosis relied on antibody testing like first-generation ELISA. These assays did not detect the virus in early infection such that before the immune system producing the antibodies. Many diagnoses were delayed, spreading disease and increased the morbidity. HCV treatment was hindered by antibody-based testing that

could not distinguish active from past infections. Nucleic acid testing (NAT) has improved HCV screening by detecting the disease sooner and improving patient outcomes[3]. NAT improves HCV sensitivity testing greater by detectingthe HCV RNA in blood samples before antibodies were produced, therefore active infections could be discovered. NAT decreases the infection window from 70 days with antibody testing to 7–10 days, benefiting high-risk populations including blood donors and organ transplant recipients. Early HCV detection may improve the efficiency of treatments by reducing the treatment period, minimizing the virus spread and increasing the patient recovery outcomes[4].

Clinicians have found NAT particularly useful in numerous cases of HCV treatment due to its capacity for early detection. NAT identifies HCV RNA in donors before the immune system has produced detectable antibodies, thus significantly reducing the window period for infection. This capability allows NAT to detect recent infections that antibody-based tests might miss, thereby ensuring that blood donations are screened more thoroughly and reducing the risk of transmitting HCV through transfusions. As a result, NAT has considerably enhanced the safety of blood donation processes by catching infections early and protecting recipients from potential exposure. The screening for organ transplant donors for HCV transmission analysis has relied on NAT. Despite its high sensitivity and effectiveness, the NAT's cost and complexity limit its adoption, especially in LMICs. NAT is impracticable in decentralized healthcare systems with limited resources since it requires lab equipment and skilled people. In these cases, less sensitive but cheaper rapid diagnostic tests (RDTs) are performed[5]. The RDTs is an alternative testingover the more complex diagnostic assays in resource-constrained locations with insufficient laboratory infrastructure. Screening organ transplant donors for HCV transmission risk has primarily relied on nucleic acid testing (NAT) due to its high sensitivity and accuracy. However, the cost and complexity of NAT limit its widespread use, especially in low- and middle-income countries (LMICs). NAT's reliance on specialized laboratory equipment and trained personnel makes it impractical in decentralized healthcare settings with limited resources. In these situations, rapid diagnostic tests (RDTs) serve as a more accessible alternative, as they are less complex and more affordable. Unlike NAT, RDTs can be administered without specialized equipment or expertise, delivering results in minutes[65]. This makes them especially useful for community health programs and mobile HCV screenings, which can test for HCV antibodies and antigens in resource-limited environments. Although RDTs are less sensitive than NAT and ELISA during early infection when antibody levels are low, they still play a crucial role in expanding HCV screening in underserved communities. Ongoing research aims to enhance RDT sensitivity in detecting the virus at low concentrations and reducing false negatives.[6].

HCV screening technology ELISA has improved since its debut. Third-generation of ELISAs detect HCV antibodies more precisely and sensitively. ELISA is used in high and low-resource settings due to its low cost, convenience of use, and ability to screen many samples fast. Like other antibody-based techniques, ELISA cannot detect HCV early in infection because antibodies take weeks to develop. ELISA cannot distinguish between current infections and viruses eliminated by therapy or spontaneous clearance. Despite these challenges, HCV screening programs, especially in moderate to high HCV incidence locations, need ELISA[7]. HCV sensitivity testing has improved, making it simpler to detect the virus early and reliably, but many barriers impede its broad adoption, especially in LMICs. Costly current testing methods like NAT are a problem. Many low-resource healthcare systems cannot afford NAT equipment, reagents, and training. Therefore, many LMICs use less sensitive testing, which may delay HCV detection and increase population transmission[8].

False positives and negatives test results complicate the HCV sensitivity testing. False negatives are a big public health hazard because patients may spread the virus without they realized it. Patients can be sufferingfrom emotional and medical distress from false positives. Diagnostic tests need for a good sensitivity and specificity to avoid mistakes. To address these issues, assays and new technologies are being refined for HCV sensitivity testing[9]. HCV sensitivity testing has cost, accuracy, and population-specific performance variations. Diagnostic assay sensitivity and specificity can be affected by age, immunological state, and HIV co-infection. Immunocompromised people may have low antibody responses, causing false-negative ELISA results. HIV-coinfected patients may have lower HCV viral levels, affecting NAT sensitivity. To make HCV screening programs effective across locales and demographics, we must address these population-specific challenges[10].

Despite these challenges, advanced HCV sensitivity testing tools work clinically. Rapid detection with sensitive assays like NAT decreases chronic HCV liver damage. Early HCV detection while viral levels are low improves treatment outcomes and reduces liver damage. Early detection and treatment reduce HCV transmission, eliminating it as a public health issue[11]. Hepatitis C sensitivity testing has improved screening and diagnosis, enabling earlier detection and better clinical outcomes. NAT and ELISA improve accuracy and sensitivity, whereas RDTs provide low-resource testing. To receive worldwide benefits from these developments, cost, accessibility, and test performance variability must be addressed. WHO advises continued research and development to overcome these constraints and eliminate HCV. By increasing HCV sensitivity testing, doctors can lessen Hepatitis C's global health impact[12].

2.0 Methodology

Many scientific studies on HCV sensitivity testing breakthroughs were investigated to provide more data and findings in the literature surveys. Peer-reviewed literature from the recent decade was reviewed for relevant information. For the newest HCV sensitivity testing advances, PubMed, Google Scholar, EMBASE, and the Cochrane Central Register of Controlled Trials were searched. These databases contain many medical and scientific research studies, making them ideal for HCV screening developments, challenges, and clinical efficacy data[13]. Searches targeted topic-specific terms. We looked for HCV sensitivity testing, screening, NAT, RDTs, and ELISA. These sentences explain HCV sensitivity testing basics, including new and old methods. The search criteria included studies on sensitivity testing technique, accuracy, and clinical uses[14].

Only high-quality, relevant studies were included due to strict criteria. To study diagnostic technology breakthroughs, implementation challenges, and clinical efficacy, HCV sensitivity testing studies were chosen. Thus, peer-reviewed research was selected for its scientific rigor. To ensure credibility, experts assess peer-reviewed articles before publishing. Studies on HCV screening program sensitivity testing in high or low-resource settings were preferred. This balanced approach revealed sensitivity testing breakthroughs and the challenges of using them across healthcare institutions[15]. Research for the review was chosen using many criteria. The inquiry began scientifically. Only rigorous and methodologically sound studies were included since they produce more reliable results. We removed studies without defined study plan, data collecting, or analysis. HCV diagnostic and therapy studies unrelated to HCV sensitivity testing were also excluded. This centered the evaluation on HCV sensitivity testing improvements[16].

Extracting data from relevant studies provided a complete HCV sensitivity testing summary. Technology, clinical efficacy, and sensitivity testing constraints in varied healthcare settings were explored during data harvest. New diagnostic tests like enhanced NAT or more sensitive RDTs were examined for their influence on HCV screening accuracy and accessibility. Clinical efficacy studies on these diagnostics, such as their ability to reduce the HCV detection window or improve patient outcomes through early identification, were prioritized[17]. A narrative review synthesized data from multiple study designs. This strategy proved useful for finding patterns and themes among studies and scientific consensus and disagreement. The study synthesized publications to assess HCV sensitivity testing and identify knowledge gaps and research areas[18].

Technology aside, the evaluation explored clinical and resource-limited sensitivity testing problems. The cost of current diagnostic technologies like NAT limits their adoption in low and middle-income countries, according to several research. Healthcare providers use cheaper, less sensitive RDTs in these situations. Also evaluated were studies on logistical and infrastructural difficulties to sensitivity testing, such as specialized equipment, skilled workers, and quality control. The lack of resources and capacity to maintain advanced diagnostic technologies makes these issues more tough in decentralized healthcare systems[19]. The review also explored how sensitivity testing affects varied groups, particularly high-risk HCV patients. Several studies addressed sensitivity testing in immunocompromised, intravenous drug, and high-prevalence groups. These studies showed how immunological condition, HIV co-infection, and socioeconomic status affect HCV sensitivity. Population-specific data is needed to understand testing methods' limitations and improve HCV screening program equality and accessibility[20].

Research biases and constraints were considered throughout data analysis. In scientific research, publication bias may have eliminated experiments with negative or inconclusive results, skewing sensitivity testing progress judgments. Study quality and design were also addressed for interpreting data, especially when studies employed different methods or focused on separate sensitivity testing components. Data constraints were considered when making conclusions and suggesting more research[21]. A balanced assessment of HCV sensitivity testing developments was the goal. The review included many reputable databases, well-defined inclusion criteria, and scientifically rigorous studies to cover HCV sensitivity testing. The review identified important innovations, challenges, and therapeutic uses of HCV sensitivity testing and identified research and development themes by meticulously accumulating and integrating data from multiple studies[22].

This evaluation was carefully designed to include the most relevant and reputable studies and extract data that accurately depicted HCV sensitivity testing advances. This study will improve HCV screening understanding and affect global research and policy to improve early detection and management[23].

3.0 Data Analysis

Hepatitis C (HCV) screening sensitivity testing advances, challenges, and clinical efficacy are examined in this study. A meta-analysis of peer-reviewed academic literature demonstrates that HCV sensitivity testing has improved dramatically in recent decades. Worldwide, HCV infection management and treatment have improved due to more accurate and fast identification. These technologies differ in use and accessibility across healthcare settings, especially between high-income and low- and middle-income countries[24]. Nucleic acid testing (NAT) transformed HCV sensitivity testing. NAT's sensitivity allows it to detect HCV RNA in blood samples before antibodies are produced. This feature dramatically reduces the time between infection and virus detection using standard antibody testing. Active HCV infections are detected faster and more accurately by NAT than by

ELISA, which uses the host's antibody response. Conventional testing takes 70 days to complete, however the NAT decreases it to 7–10 days, according to studies. In blood donation and organ transplantation, early detection can save lives, therefore this development is vital for decreasing virus transmission[25].

Given its high cost and technological complexity, NAT is rarely employed, especially in resource-limited situations. LMICs face high costs for NAT reagents, equipment, and skilled labor. These areas lack funds and infrastructure to use modern testing techniques. Thus, NAT is the gold standard in many high-income nations but infrequently employed in LMICs, resulting in early detection rate differences. This disparity highlights the need for cheaper, more accessible diagnostic methods with comparable sensitivity[26]. NAT is often replaced with rapid diagnostic tests (RDTs) in areas with few labs. With minimal equipment and training, RDTs yield results in minutes. They detect HCV antibodies or antigens, making them excellent for rural or underserved point-of-care testing. Many research in this review suggested that RDTs are getting more accurate, especially with newer tests with improved sensitivity and specificity. Despite these advances, RDTs are less sensitive than NAT early in infection when antibody levels are low[27].

RDTs' poorer sensitivity to early infections is a serious downside, especially in high-risk populations where early intervention is critical. Intravenous drug users and HIV co-infected patients may have low viral loads or altered immune responses, causing false-negative RDT results. RDT false positives may upset patients and necessitate more testing. RDTs have increased LMIC HCV testing, but technical advances must address the cost-sensitivity trade-off[28]. ELISA technological development is also significant. In significant public health projects, ELISA has been employed for HCV screening. Newer ELISA methods detect HCV antibodies more precisely and sensitively. The low cost, simplicity, and speed of these tests make them popular. ELISA allows quick, reliable testing of large volumes in blood donor screening. Like all antibody-based methods, ELISA cannot detect HCV early in infection. This weakness underlines the need for more sensitive HCV early detection methods[29].

Several studies show that combining diagnostic approaches improves HCV screening program sensitivity. Combining ELISA and NAT or screening with RDTs and NAT improves early infection identification. This tiered approach allows persons who test positive with less sensitive testing to be investigated with more sensitive procedures in resource-limited situations. This could assist overcome testing method limits and give a more thorough and effective screening solution[30].This review shows that better sensitivity testing methods are clinically effective beyond technological advances. Early identification helps treat HCV and prevent cirrhosis and liver cancer. Early therapy start enhances clinical results for sensitive procedures like NAT, according to studies. Early diagnosis lowers communal HCV transmission, especially in high-prevalence locations. The excellent cure rate of direct-acting antiviral (DAA) therapy emphasizes early detection. Early DAA treatment can prevent liver damage and improve quality of life for chronic HCV patients[31].

Early detection provides clinical benefits, but sensitive testing is hard to achieve. LMIC study shows that cost, infrastructure, and logistics limit general use of contemporary diagnostic methods. These healthcare practitioners employ antiquated, less sensitive equipment that miss early-stage illnesses, delaying treatment and increasing transmission risk. The literature consistently demands for affordable, high-sensitivity, low-cost point-of-care diagnostics, showing a need for greater research and innovation[32]. In addition to cost and accessibility, this study examines population test performance variability. Several studies demonstrate that age, immunological state, and co-infection with other viruses can reduce HCV test sensitivity. Immunocompromised people like HIV co-infected people may fail ELISA testing due to low antibody levels. Population differences affect NAT and RDT performance like viral load. These findings highlight the need to tailor HCV screening programs to demographic groups, particularly those at higher risk[33].

Statistics also highlight the need for quality control and training to appropriately execute and evaluate sensitivity tests. Resource-constrained environments with insufficient infrastructure and competence increase testing and diagnosis errors. This review emphasizes the importance of ongoing training for healthcare professionals and laboratory staff and thorough quality control to ensure test findings reliability. False positives and negatives must be reduced to improve HCV screening systems[34]. HCV sensitivity testing has increased diagnosis accuracy and timeliness, increased clinical outcomes and reducing transmission risk, according to studies. But cost, accessibility, and population-specific test performance remain important challenges. NAT is the gold standard for early detection, but its expense and complexity prevent many countries from using it. RDTs and ELISA increase testing access, but their sensitivity limits, especially in early infection, require further innovation. By solving these problems and improving sensitivity testing, future research can eradicate HCV as a global health issue[35].

4.0 Advances in Sensitivity Testing for HCV

Nucleic Acid Testing (NAT) has revolutionized HCV sensitivity testing by detecting the infection early with unprecedented precision. Instead of antibodies, NAT directly detects HCV RNA in blood, revealing active infections before the immune system can produce antibodies. NAT reduces the time between infection and virus detection from 70 days to 7–10 days. Blood donation and organ transplants require early detection to prevent

viral transmission, making this advancement vital. Early NAT identification stop HCV spread and allow earlier medical intervention, improving patient outcomes and decreasing liver damage[36]. Antibody-based tests may miss infections; however NAT can detect even low amounts of HCV RNA. This is crucial for people with low viral loads or acute infection, where antibody production has not begun. Thus, in high-risk populations like blood donors and organ transplant patients, NAT is the best HCV test. The technology behind NAT is amazing, but its implementation is tricky. NAT is complicated and expensive, requiring advanced lab equipment and trained testers and interpreters. These operational considerations have hampered NAT deployment, especially in LMICs with limited healthcare resources. These settings use cheaper, less sensitive testing procedures that can overlook early-stage illnesses and delay treatment[37].

NAT enhanced HCV sensitivity testing, but cost and infrastructure have made rapid diagnostic tests more accessible. RDTs are popular for their speed, simplicity, and low cost. In resource-limited environments with limited laboratory infrastructure, these tests can be given at the point of therapy without specialist equipment or highly experienced people. Population screening and community health programs benefit from RDTs that detect HCV antibodies or antigens. RDTs are a feasible strategy to boost screening in high-HCV areas[38]. RDTs are faster and more accessible than NAT, but their poor sensitivity restricts them in early infection. RDTs are less successful at detecting infections due to poor acute antibody production. HCV-infected people may get false-negative tests. In high-risk populations like drug injectors and HIV co-infected people, early detection and treatment limit virus spread. False RDT positives can upset patients and require additional testing to diagnose. Though challenging, RDT technology is advancing, with newer tests having higher sensitivity and specificity. RDTs may become more important in global HCV screening efforts, especially in places where cost and infrastructure limit sophisticated testing methods[39].

Still widely used for HCV sensitivity testing is the enzyme-linked immunosorbent assay (ELISA). Blood samples have been screened for HCV antibodies using ELISA for decades. Its high sensitivity, specificity, and speed in screening multiple samples keep it popular. ELISA works well for chronic HCV infections with high antibody levels and an established immune response. Third-generation ELISA assays are accurate enough for blood donation screening and other large-scale testing[40]. RDTs and ELISA rely on the host's immune system's virus-specific antibodies, which restricts detection. ELISA may miss HCV during the acute phase because to the immune response. Thus, HCV-infected persons without antibodies may have false-negative results, delaying diagnosis and treatment. Early detection for viral prophylaxis is crucial in high-risk populations, making this constraint significant. After treatment or spontaneously, ELISA cannot distinguish between ongoing and cleared infections. This inability to distinguish between present and former infections may make test results difficult to interpret and require additional testing to confirm infection status[41].

ELISA is still relevant in HCV screening programs, especially in moderate to high HCV prevalence locations where many persons must be examined fast. ELISA's low cost and great throughput make it popular in HCV control programs. Screening with ELISA and validation with NAT is common in high-resource circumstances. ELISA is a cost-effective first line of defense for HCV infection risk assessment and referral to more conclusive testing and therapy[42]. Finally, HCV sensitivity testing has substantially improved early detection, enabling timely treatment. NAT is the gold standard in early-stage HCV diagnosis due to its high sensitivity in detecting HCV RNA, but its cost and technical complexity limit its use in resource-constrained scenarios. RDTs are easier to use but have poorer acute infection sensitivity, resulting in false negatives. ELISA is useful for large-scale screening despite its inability to detect early-stage infections and distinguish between current and former illnesses. These technologies offer advantageous and disadvantageous HCV screening options. By improving these testing methods, fast HCV diagnosis and more accurate results can be obtained.[43].

5.0 Nucleic Acid Testing (NAT)

Nucleic Acid Testing is a cutting-edge of Hepatitis C virus sensitivity test. Its direct detection of viral RNA rather than the host's antibody reaction has revolutionized HCV early detection. NAT detects active infections ahead of antibody-based assays, which require weeks or months. This substantial reduction from 70 days with conventional approaches to 7 to 10 days with NAT is essential for limiting virus transmission in high-risk groups like blood donors, organ transplant patients, and healthcare personnel exposed to contaminated instruments[44]. Early HCV symptoms are usually silent, leading to its stealthy spread. Unsymptomatic people can accidentally spread the virus. Problematic are medical settings that use infected blood or organs before normal screening detects the infection. HCV can be detected early by NAT's viral RNA detection in blood or other biological materials. Hospital screenings prevent HCV from spreading to patients and staff, therefore early diagnosis interrupts the transmission cycle[45].

NAT's sensitivity improves blood donor screening. Blood banks used antibody-based testing, which worked for older illnesses but not recent ones. A donor with long-term HCV infection would have negative blood tests due to insufficient antibody development. NAT can detect HCV RNA days after infection before antibodies appear, reducing this risk. Countries that employ NAT for routine blood screening have considerably improved blood safety[46]. A major feature of NAT is its ability to identify very low viral RNA levels. Low viral loads can

transmit the infection without causing symptoms or activating an immune response, making this crucial. Low viral loads are common in early HCV infection or HIV co-infected persons. Medical intervention and transmission reduction have increased due to NAT's early detection of low-level illnesses[47].

NAT is essential for organ transplantation. Antibody-based diagnostics missed donor organ HCV infections before NAT was widely utilized, increasing transplant recipients' risk. The urgency of many transplant procedures led to the use of organs from infection window donors, spreading HCV. NAT screens donor organs for HCV RNA, detecting early infections before transplantation. This has considerably improved organ transplant safety and success and reduced post-transplant HCV infections[48]. NAT has many benefits but is hard to deploy. NAT is more expensive than antibody-based diagnostics, limiting its use in LMICs with limited healthcare resources. With its substantial laboratory infrastructure, specialized equipment, and highly qualified people, NAT costs more. Financial and logistical obstacles prevent many LMICs from using NAT in regular HCV screening. Healthcare providers utilize less sensitive, cheaper testing procedures in these places, delaying virus detection and HCV control[49].

The test is invaluable in centralized labs that can handle NAT expense and complexity. High-income countries with well-developed healthcare systems use NAT in HCV screening processes, especially in blood banks, organ transplant centers, and immunocompromised patient care facilities. The patient safety and infection control benefits from NAT justify its higher cost in these settings. NAT has reduced transfusion-transmitted HCV in nations that utilize it for blood screening, safeguarding the blood supply[50]. NAT test results must be interpreted. Although sensitive and specific, NAT may yield false-positive or false-negative results. Though rare, sample contamination during collection or processing might generate false positives, stressing patients and requiring follow-up testing. Individuals with extremely low viral loads below the test's detection threshold may have false negatives. These issues emphasize the requirement for quality control and testing protocol monitoring to ensure NAT results accuracy and reliability. In centralized labs, such controls prevent errors, but in resource-limited contexts, they may be challenging to maintain[51].

NAT's clinical benefits outweigh its downsides. Early HCV identification allows for immediate antiviral treatment, which slows disease progression and reduces cirrhosis and liver cancer risk. Early diagnosis helps public health programs limit HCV transmission, especially in endemic areas. By recognizing infections during the acute phase, when virus levels are highest, NAT terminates transmission chains and protects susceptible populations[53]. Another notable effect of NAT is on HCV treatment outcomes. NAT-diagnosed HCV patients have a higher SVR rate after direct-acting antiviral therapy. SVR indicates therapeutic success by eliminating the virus from the patient's bloodstream. NAT can identify HCV RNA before symptoms or liver damage, allowing patients to start therapy early and boost their SVR potential and reduce chronic HCV infection risks[54].

Early virus detection by NAT revolutionizes HCV sensitivity testing. The ability to identify HCV RNA before antibodies are produced has revolutionized HCV diagnosis and treatment, especially in high-risk populations like blood donors, organ transplant recipients, and immunocompromised patients. NAT is essential in centralized laboratories where early detection overcomes installation costs, but LMICs have limited its usage due to its cost and complexity. This revolutionary technology may become widely available internationally as healthcare systems improve and NAT costs decline, helping control and eliminate HCV as a serious public health issue[55].

6.0 Rapid Diagnostic Tests (RDTs)

HCV Rapid Diagnostic Tests (RDTs) are popular due to their accessibility, convenience of use, and short turnaround times. RDTs are a cost-effective alternative to Nucleic Acid Testing (NAT) in many contexts, especially those without lab facilities. RDTs are less sensitive than NAT for early detection, although recent developments have improved their HCV antibody or antigen detection[56]. Medical resources and centralized laboratory testing are few in low- and middle-income countries (LMICs), making RDTs important. Decentralized RDTs can be used in rural, mobile, and primary care. Healthcare providers screening large populations or diagnosing patients in one visit value their ability to provide results in minutes to hours rather than days or weeks. Immediacy also lowers loss to follow-up, which can be a major concern in HCV therapy, especially in areas where patients have poor healthcare access or must travel far to get results[57].

Usability and simplicity are RDTs' goals. Healthcare professionals with minimal training can perform RDTs, but NAT requires special equipment and staff. Most RDTs detect HCV antibodies or antigens using a fingerstick blood sample on a test strip. A positive test strip line, like a home pregnancy test, demonstrates HCV exposure. Only test strips and buffer solutions are needed to test in minutes. Simple RDTs are necessary for scaling HCV screening in places with inadequate healthcare infrastructure[58]. Despite these benefits, RDTs have downsides, especially HCV detection sensitivity. RDTs are less sensitive than NAT early in infection, a key downside. Because they detect HCV immune responses via host antibodies or viral antigens, RDTs are less accurate at detecting new infections. Patients can test negative for HCV for weeks following infection due to antibody formation. False-negative RDTs delay diagnosis and treatment[59].

False negatives are especially concerning in high-risk populations like intravenous drug users and HIV co-infected patients since early detection and treatment reduce viral infections. HIV-co-infected persons may have weak HCV antibodies, resulting in false-negative RDT results. Infected persons with low virus loads from early infection or antiviral therapy may test negative. These limitations emphasize the importance of verifying RDT results with more sensitive tests like NAT when clinical suspicion of HCV remains high[60]. Rarely, RDTs can yield false-positive results. False positives can result from virus or protein cross-reactivity, poor test management, or test strip issues. Although false positives do not pose health risks, they waste follow-up testing, patient stress, and healthcare system costs. Most healthcare practitioners recommend NAT or other sensitive diagnostic testing for positive RDT results. Initial screening with RDTs and confirmatory testing with NAT improve HCV screening program accuracy, especially in resource-limited settings[61].

Despite these limitations, RDTs are essential for extensive HCV testing. Large-scale screening and diagnosis are only possible using RDTs in many countries, notably LMICs. RDTs can be utilized in urban and rural health facilities without expensive equipment or trained staff to increase HCV tests. RDTs must be available to drug injectors and the uninsured. On-the-spot RDT results speed diagnosis and treatment[62]. Advanced RDT technology has also improved sensitivity. New RDTs can detect HCV early with enhanced antibody and antigen sensitivity. RDTs that test antibodies and antigens on one strip can detect infections even with low antibody levels. These improvements may improve early-stage infection detection and reduce false negatives in RDTs. Research on point-of-care molecular diagnostics that can identify viral RNA without lab equipment may also close the RDT-NAT sensitivity gap[63].

Their affordability also makes RDTs popular. Although NAT is sensitive, routine screening in LMICs, especially rural or impoverished regions, is expensive. Due to their low cost, mass screening programs may afford RDTs. For their price and convenience, RDTs' lower sensitivity is generally accepted, especially in screening as many individuals as feasible. RDTs for preliminary screening and confirmatory testing for positive cases are cost-effective HCV detection approaches[64]. RDTs may increase healthcare patient engagement. Patients can discuss treatment options and follow-up therapy immediately after RDTs are interpreted. Immediacy decreases exam anxiety and encourages health management. Traditional laboratory testing may require patients to return, delaying diagnosis and treatment and increasing follow-up loss[65].

RDTs are less sensitive than NAT at detecting early-stage HCV infections, but they have expanded testing, especially in resource-limited locations. They are crucial to global HCV screening efforts due to their accessibility, ease of use, and short turnaround time, especially in areas lacking proper laboratory facilities. RDT technology improves sensitivity and reliability, but false-negative and false-positive readings persist. As sensitive and economical diagnostic technologies are developed, RDTs will certainly help identify infected patients and curb HCV spread[66].

7.0 Enzyme-Linked Immunosorbent Assay (ELISA)

HCV screening with the Enzyme-Linked Immunosorbent Assay (ELISA) is popular worldwide. HCV diagnosis, especially large-scale screening, has relied on ELISA's outstanding sensitivity and specificity in detecting HCV antibodies since its launch. Test accuracy and reliability have increased with each generation. Third-generation ELISAs are more accurate, especially for persistent HCV infections. This accuracy has strengthened ELISA's place in the HCV fight, diagnosing many at-risk individuals[67]. ELISA is useful for detecting HCV antibodies, which the body creates in response to the infection. HCV-specific antibodies are generated by the immune system and detected by ELISA. A valuable chronic HCV detection tool, the third-generation ELISA can detect even low levels of these antibodies due to its high sensitivity. Those who have had the virus for years without symptoms need this sensitivity. Early HCV cases are often asymptomatic, allowing the virus to spread undetected. Untreated chronic infections can cause cirrhosis and liver cancer. ELISA's precision in detecting HCV antibodies helps doctors diagnose infections early[68].

Though frequently used and successful, ELISA has limits. Detecting antibodies rather than viruses is a drawback. ELISA detects HCV's immune response, not its presence. Chronic infections are detected well, whereas acute HCV is not. An individual may be infected but test negative on an ELISA early in HCV infection because the body has not produced enough antibodies. This antibody synthesis delay can cause weeks-long false-negative results during acute illness. Thus, newly infected people may not be diagnosed until the infection has established, reducing early care and transmission risk[69]. In addition to the window period, ELISA has problems discriminating current and past infections. The antibody test cannot establish if the infection is active or if the person has cleared the virus through treatment or spontaneous remission. Due to this inability to distinguish previous and present infections, diagnosis may require additional tests. Medical professionals use ELISA as a screening method, then nucleic acid testing (NAT) to confirm infection. In high-prevalence HCV settings with large populations to screen quickly, ELISA is still commonly utilized as an initial screening tool despite these issues[70].

Its convenience and cost-effective make ELISA popular in HCV screening programs. ELISA is cheaper and easier to deploy than NAT for large-scale public health activities. HCV control requires low-cost screening of

large numbers of persons in moderate to high prevalence countries. ELISA's high throughput allows it to analyze multiple samples at once, making it perfect for blood donation centers, hospitals, and other healthcare facilities that need speedy screening. ELISA is the first line of defense for HCV infection, allowing prompt referral to confirmation tests and treatment[54]. Third-generation ELISAs have good sensitivity and specificity, especially for chronic HCV infections, reducing false-positive and false-negative results. Healthcare facilities need this diagnostic precision since misdiagnoses might hurt patients. A false-positive could stress the patient and need costly follow-up testing, while a false-negative could delay treatment and increase transmission risk. Healthcare practitioners and public health officials trust third-generation ELISA because it decreases errors[32].

ELISA and healthcare have been used to screen blood donors. ELISA has reduced HCV transmission through blood transfusions, and healthcare systems globally prioritize blood supply safety. ELISA tests blood for HCV antibodies to prevent infected blood from entering the supply chain and jeopardizing recipients. Due to its excellent sensitivity and specificity, the third-generation ELISA may detect HCV antibodies in low concentrations. Despite improved blood safety methods like NAT, ELISA is still utilized for first screening because to its cost-effectiveness and ease of use[29]. ELISA offers several benefits, but research is underway to improve its early HCV detection. Diagnostic advances include sensitive assays and point-of-care diagnostics aim to reduce the window period and improve acute HCV detection. These advancements may enhance or replace ELISA in high-risk populations when early detection prevents viruses. ELISA will be essential for HCV screening until these new technologies are widely available[65].

The Enzyme-Linked Immunosorbent Assay (ELISA) is essential for HCV screening due to its high sensitivity and specificity in detecting HCV antibodies. The third-generation ELISA is more accurate in chronic infections, but its antibody detection approach makes acute infections problematic. Although limited, ELISA is widely used in HCV screening programs, especially in moderate to high incidence nations. Large-scale screening programs need an accessible, cost-effective, and reliable way to diagnose and recommend HCV-risk individuals for testing and treatment. ELISA's position in HCV screening may vary as diagnostic technology advances, but its diagnostic contributions are crucial[68].

8.0 Innovations

HCV sensitivity testing's clinical success is linked to diagnostics developments in recent decades. Early HCV discovery, especially acutely, improves patient outcomes and minimizes transmission. Early intervention with reliable diagnostics can prevent liver disease progression including HCV-related cirrhosis, liver failure, and hepatocellular carcinoma. Diagnostic technologies are evolving to make healthcare testing more sensitive, accessible, and efficient[45].An important HCV sensitivity testing advancement is Nucleic Acid Testing (NAT). NAT revolutionised early HCV infection detection by directly identifying viral RNA, often before antibodies emerged. This discovery may identify HCV within 7 to 10 days of infection, unlike antibody-based assays of much longer duration. For high-risk populations and those in the acute phase of illness, early intervention is critical for health outcomes and transmission prevention. NAT can detect even tiny amounts of viral RNA[39].

Further NAT technology improvements have increased test efficiency and accessibility. Automation of NAT systems speeds up testing and diagnostic lab throughput. These technologies allow healthcare facilities to quickly handle big samples, making NAT better for mass screening. NAT assay sensitivity improvements have reduced false negatives and increased early detection. Innovations like these make NAT the gold standard for HCV detection in high-resource locations with the infrastructure[47]. NAT's cost and complexity restrict its widespread use in LMICs with limited healthcare resources. Due to this issue, scientists and healthcare innovators are exploring cheaper, more accessible NAT alternatives with high sensitivity and specificity. Innovations include point-of-care molecular assays. These assays offer NAT accuracy and early detection to resource-limited situations without specialist laboratory equipment. Point-of-care molecular testing is rapid, portable, and requires no sample transfer to labs. This research could considerably improve early HCV diagnosis in rural and poor settings, where treatment and infection prevention are essential[50].

Clinical HCV sensitivity testing has improved with RDTs and molecular testing. RDTs are less sensitive than NAT in early-stage infections because they identify HCV antibodies or antigens rather than viral RNA. Recent RDT innovations have increased sensitivity and specificity. Dual-detection RDTs detect antibodies and antigens on one strip. This development makes RDTs useful for large-scale screening programs in resource-limited locations by detecting early-stage diseases[57]. RDTs are affordable and accessible. They are inexpensive, easy to use, and can be delivered at the point of care without training or equipment. LMICs, where healthcare infrastructure is lacking and centralized NAT laboratories are impossible, benefit from RDTs. Scaling up HCV screening in high-prevalence locations requires fast, cheap population screening. RDTs improve patient outcomes and reduce HCV load on healthcare systems by improving testing access[42].

HCV sensitivity testing is more effective with AI and machine learning. AI-driven diagnostic tools can uncover patterns and correlations in huge datasets that humans miss, enhancing HCV testing accuracy and efficiency. AI algorithms can read diagnostic test results more accurately, reducing human error. AI-powered diagnostic systems can identify HCV-risk patients based on medical history, demographics, and behavior. AI can improve

patient outcomes by optimizing screening programs to find high-risk patients early and properly[35]. HCV sensitivity testing has been improved with NGS technologies, which are more sensitive and specific. NGS allows comprehensive HCV genome analysis, revealing its genetic makeup and variations. When a virus has evolved to resist antiviral treatment, this level of precision is crucial. Early genetic variant detection helps doctors tailor treatment to each patient, improving outcomes. NGS can detect tiny levels of viral RNA that conventional methods miss, enhancing early HCV diagnosis[33].

HCV sensitivity testing in public health programs has also enhanced clinical efficacy. Many locations include HCV screening in HIV, TB, and maternal health programs. Healthcare providers can use existing infrastructure and resources to boost HCV testing, especially in vulnerable groups, with this integrated strategy. By combining HCV screening with other routine healthcare services, healthcare organizations can reach at-risk individuals who may not otherwise test. This method increases HCV sensitivity testing and results in faster and more accurate diagnosis, allowing for early intervention and better health outcomes[26]. Maintaining universal access to sensitive HCV testing procedures is problematic despite these advances. Technological developments have improved HCV diagnostic accuracy and efficiency, but cost, especially in LMICs, prevents widespread usage. In resource-limited settings, building NAT, NGS, or point-of-care molecular testing infrastructure is costly, hence healthcare organizations may adopt less sensitive, cheaper RDTs. To address this issue, international health organizations and governments must cut the cost of innovative diagnostic equipment and make it more accessible to resource-limited healthcare providers[29].

Diagnostic tool accuracy, accessibility, and efficiency have greatly improved HCV sensitivity testing clinical effectiveness. NAT, RDTs, AI-driven diagnostics, and NGS increase HCV infection detection and provide rapid treatment to improve patient outcomes and reduce transmission. These innovations and integrated public health activities have expanded HCV screening programs, especially in high-prevalence areas where early detection is critical. Developing cheaper and more accessible HCV testing methods may improve diagnoses and lower the global disease burden[30].

8.1. Nucleic Acid Testing (NAT)

The groundbreaking Nucleic Acid Testing (NAT) directly detects viral RNA in blood samples, finding active HCV infections earlier than antibody-based assays. The "window period" between HCV infection and discovery is greatly reduced by NAT's early detection. Compared to antibody testing, NAT detects HCV RNA 7–10 days post-infection, making it a very sensitive method for detecting HCV before antibodies emerge. This breakthrough allows healthcare providers to intervene earlier in the infection timeline, improve patient outcomes, and restrict virus propagation, especially in high-risk groups[45].In addition to early detection, NAT has improved blood donation and organ transplantation safety. Before NAT, antibody-based assays had a detection gap, especially for recent infections without an immune response. NAT's capacity to detect viral RNA in blood donors and organ transplant candidates reduces HCV transmission across these important pathways[51]. Blood banks and transplant facilities in high-income countries use NAT to test blood and organs for HCV before antibodies emerge. This proactive screening method has dramatically improved blood supply safety and reduced post-transplant HCV infections, safeguarding donors and recipients.NAT is clinically beneficial but difficult to implement, especially in low- and middle-income countries. For accuracy, the test requires lab equipment, skilled workers, and controlled settings[23]. These constraints make NAT expensive and technically difficult, making it only practical in centralized or well-funded healthcare systems. In LMICs with limited healthcare resources and infrastructure, NAT's high cost and operational complexity hinder implementation. As a result, many LMICs use less sensitive diagnostic technologies that are faster to implement but risk missing early-stage illnesses[42].Research and development to make NAT more accessible and economical for resource-constrained contexts continues. Innovative methods like point-of-care molecular testing aim to give NAT's sensitivity in more portable, less resource-intensive formats for decentralized or rural healthcare. These advances are promising, but global NAT access is difficult. Increasing NAT availability and cost could enhance HCV testing standards worldwide, enabling earlier diagnosis, better patient outcomes, and better global HCV transmission management[61].

8.2. Rapid Diagnostic Tests (RDTs)

Rapid Diagnostic Tests (RDTs) are a realistic alternative to NAT in resource-limited environments where healthcare infrastructure may not support advanced diagnostic methods. RDTs are simple and easy to administer, so healthcare professionals can do so without specific lab equipment or training. In LMICs, rural areas, and mobile healthcare programs where lab resources are scarce, RDTs are used for initial HCV screening since they yield results in minutes rather than days. They are easy to use and affordable, making them suitable for large-scale screening programs, such as community health initiatives targeting high-prevalence and high-risk populations.RDTs are versatile in decentralized and distant healthcare settings with limited infrastructure[12]. HCV antibodies or antigens are usually detected by fingerstick blood samples in RDTs. This allows them to be useful in community health programs, outreach campaigns, and settings where patients may only see one doctor.

RDTs provide wider screening and early HCV detection in populations with limited access to conventional medical services.Although useful, RDTs have limitations that lower their sensitivity, especially early in infection. RDTs use antibodies or antigens, which the body may take weeks to generate after infection, unlike NAT, which detects viral RNA[24]. Thus, RDTs may give false negatives in recently infected HCV patients without antibody levels. Early intervention is essential to avoid disease progression and transmission in high-risk groups, but this sensitivity limitation makes it difficult. RDTs can also give false positives due to cross-reactivity with other illnesses or diseases, requiring unnecessary confirmatory testing and causing patient concern[34].Recent RDT developments have improved sensitivity and specificity to overcome these limitations. Dual-detection RDTs can detect HCV at different stages of infection since they detect antibodies and antigens. RDTs are becoming more sensitive to NAT, but they cannot match its early detection capabilities. However, RDTs' cost-effectiveness and accessibility make them useful for early screening in resource-limited situations. As technology advances, RDT sensitivity and specificity could improve HCV diagnosis, increasing access to testing and enabling faster responses to new infections in understocked areas[56].

8.3. Enzyme-Linked Immunosorbent Assay (ELISA)

ELISA has long been used for HCV screening in high-volume testing situations like blood banks, public health initiatives, and hospitals. Blood ELISA tests detect HCV antibodies, making them useful for chronic infection detection and high-prevalence population screening. ELISA's third-generation assays are more sensitive and selective and cheaper. ELISA's significance as a major HCV screening technique has strengthened, especially in moderate to high-prevalence locations where large numbers of people must be screened efficiently[34].ELISA is ideal for high-throughput testing because it can handle huge sample volumes without human interaction. ELISA can handle hundreds to thousands of samples in a batch, making it useful in centralized laboratories, blood donation facilities, and at-risk screening programs. ELISA is simple and inexpensive, making it a good choice for many healthcare settings, particularly those with limited resources, to identify patients who may need additional testing or treatment.

ELISA's antibody detection makes early-stage HCV diagnosis difficult. Since antibodies form slowly after infection, ELISA may give false-negative results in recent HCV exposure patients without antibodies[47]. ELISA is less successful for early-stage detection, which is a major drawback for high-risk populations where early intervention is essential to avoid disease development and transmission. ELISA detects the immune system's response, not the virus, hence it cannot discriminate between ongoing and prior infections. Thus, people who have cleared the virus naturally or through therapy may still test positive, necessitating further testing to confirm their infection status[24].Due to its cost-effectiveness, simplicity, and scalability, ELISA is commonly utilized in HCV screening programs despite these drawbacks. ELISA is commonly used as the initial screening test and NAT confirms positive cases in high-resource settings to balance cost and accuracy. ELISA balances cost and precision, making it ideal for large-scale screening programmes, especially in LMICs. ELISA will likely remain a key technique in HCV screening as diagnostic technologies improve, especially when more sensitive and economical early detection approaches are developed[29].

9.0 Challenges in Sensitivity Testing

Hepatitis C virus (HCV) sensitivity testing is still difficult to employ, especially in resource-limited settings. Nucleic Acid Testing (NAT) and Rapid Diagnostic Tests (RDTs) increase detection and diagnosis, but cost, accuracy, accessibility, and variability limit their efficacy. These restrictions must be solved to strengthen global HCV screening programs and deliver early and accurate detection to all regions, independent of resources[37]. In low- and middle-income nations, HCV sensitivity testing is difficult to access. Many regions cannot afford NAT testing, which detects HCV infections earlier and more sensitively. NAT requires expensive reagents, lab equipment, and expert lab operators to interpret results. Many LMICs lack NAT infrastructure due to decentralized healthcare systems. Many hospitals use first-generation ELISA or basic antibody assays because they cannot give sensitive tests. These inexpensive methods often hinder HCV early identification, especially in high-risk populations where the virus must be diagnosed before it develops chronic infection. Due to the cost-accuracy trade-off, improving global HCV screening programs is difficult[39].

Cost makes RDTs a popular alternative to NAT in LMICs. RDTs are cheap, rapid, and easy to use, making them suitable for resource-constrained healthcare providers. RDTs are beneficial for scaling up screening in rural areas, although they are less sensitive than NAT, especially early in disease when the viral load is low or antibody production has not begun. This makes it harder to detect HCV infections, which is essential for virus control. RDT sensitivity has improved, especially with newer antigen assays, yet the accuracy gap between RDTs and NAT remains. Infected people who test negative on RDTs may delay treatment[46]. HCV sensitivity testing is limited by false positives and negatives, affecting patient care and public health. Misdiagnosis of infection as a false negative can be dangerous. After a false-negative test, HCV treatment may be delayed, allowing the virus to spread and increase risk. Not identifying and treating false-negative results is especially risky for drug injectors and HIV co-infected people, who are more likely to spread the illness. Early infection or

antiviral treatment that lowers HCV levels to undetectable levels can also cause false negatives. RDTs and antibody-based assays with lower sensitivity may miss infections, delaying diagnosis and treatment[57].

HCV misdiagnosis might cause psychological stress and medical procedures. If they fear they have a life-threatening infection, false positives might cause anxiety. It may require expensive and time-consuming diagnostics. Following up on false-positive results might burden healthcare systems due to funding restrictions. False-positive results can lead to unnecessary antiviral treatment, adverse effects, and costs. Diagnostic tool development must prioritize HCV sensitivity tests with high sensitivity and specificity[50]. HCV sensitivity testing is complicated by population variability. Age, immunology, and HIV co-infection affect sensitivity and specificity. Immunocompetent people may acquire more HCV antibodies than HIV patients. This can cause false-negative results in HCV antibody testing like ELISA. Direct viral RNA detection methods like NAT are more accurate in these groups. NAT is expensive and difficult, thus decentralized healthcare rarely uses it. Chronic liver disease such severe cirrhosis might alter immune responses, rendering antibody-based tests inaccurate[55].

Besides immunological state, age and location can affect HCV test findings. Research suggests that elderly persons may have altered antibody levels, which can affect test sensitivity. Regional differences in HCV genotype prevalence can alter test results since some tests are more sensitive to specific genotypes. Standardizing HCV screening programs across communities is problematic since tests that work in one community may not in another. This heterogeneity underscores the importance of tailoring screening programs to the group being studied to use the most accurate diagnostic tools and reduce false results[52]. HCV sensitivity testing accuracy, accessibility, and price are being addressed through research and innovation. Cost-effective, decentralized NAT and RDT sensitivity improvements are needed to boost HCV screening availability. Also promising for resource-limited situations are point-of-care molecular diagnostics that identify viral RNA without advanced lab equipment. By coupling price and accuracy, these tests could help doctors diagnose HCV infections early and accurately regardless of location or resources[57].HCV sensitivity testing has improved, but many barriers impede its widespread adoption, especially in resource-limited settings. Accessibility, cost, false positives and negatives, and population-specific test performance hinder HCV screening efforts. Research and innovation are needed to improve global HCV detection and assure early and accurate diagnosis[62].

9.1. Accessibility and Cost

Modern Hepatitis C virus (HCV) sensitivity testing technologies are difficult to utilize in low- and middle-income countries due to cost and access. HCV screening has improved with Nucleic Acid Testing (NAT), but its high cost and infrastructure constraints limit its availability. Decentralized healthcare systems with scarce resources and widespread facilities make this harder. Advanced diagnostic tests, specialized equipment, and skilled practitioners are expensive and hard to get in LMICs, where HCV infection is highest[68]. NAT is the best HCV detection method since it can detect viral RNA in blood samples early on. Early detection provides prompt treatment, preventing sickness progression and transmission. A NAT setup is costly. This test requires expensive, high-maintenance lab equipment including automated sample processing and amplification. NAT requires trained operators of complex apparatus and results analysts. These challenges hamper NAT deployment in LMICs with underfunded and overburdened healthcare systems. Most hospitals in these areas cannot afford the equipment, and the lack of qualified laboratory staff makes NAT testing programs unsustainable[70].

The cost barrier exceeds NAT configuration. NAT test kits and reagents are expensive and must be renewed. Long-term operational costs for NAT increase, burdening resource-constrained healthcare organizations. NAT equipment is stored in centralized laboratories, making sample movement difficult and expensive. Transporting blood samples to NAT-equipped labs may delay diagnosis and treatment in decentralized healthcare systems because many patients reside far from cities, negating early detection's major usefulness. Due to logistical challenges, NAT is less practical in LMICs, especially rural and remote areas with few healthcare services[63]. Rapid Diagnostic Tests are cheaper and easier to implement than NAT, hence many LMICs utilize them. These conditions favour RDTs because they are cheap, simple, and don't require lab infrastructure. Healthcare workers with minimal training can administer most RDTs at the point of service, making them ideal for screening large populations in resource-constrained locations. Despite their cheap and accessibility, RDTs have downsides. RDTs are less sensitive than NAT in early HCV infection when the viral load is low or antibodies are not yet produced. RDTs may miss early infections, delaying diagnosis and spreading[65].

LMIC HCV care differs from high-income nations due to the use of less sensitive diagnostic technology such RDTs. In well-funded healthcare systems, NAT's precision allows early diagnosis and action. LMIC patients, where RDTs are more common, may have delayed acute diagnosis. This mismatch highlights global health inequities, as economic resources determine access to cutting-edge diagnostic technology. This mismatch harms HCV patients and escalates healthcare expenses by delaying discovery[69].

LMIC test quality and RDTs' inability to detect early-stage infections are problems. RDT accuracy varies greatly by brand and test. Cheap RDTs purchased by cash-strapped healthcare organizations may have lower sensitivity and specificity, leading to more false negatives and positives. LMICs with low confirmatory testing

resources struggle with HCV screening programs due to test performance variance. False-negative results may postpone treatment until the disease is advanced, while false-positive results may waste healthcare resources on unnecessary testing or treatment[47]. NAT cost reduction and LMIC high-sensitivity testing method accessibility are needed to close these gaps. Point-of-care molecular testing that matches NAT's sensitivity without lab infrastructure may work. These early-stage assays use portable equipment to remotely identify viral RNA at the point of care. Point-of-care molecular diagnostics could revolutionize LMIC HCV screening by removing centralized labs and sample transportation. These technologies may cost more than RDTs and are not widely available[45].

Meanwhile, RDT sensitivity is improving. New RDTs that detect antibody and antigen on one test strip are being developed to better detect early-stage infections. RDTs may be a better LMIC HCV screening option if NAT is not viable due to these developments. International health organizations' NAT funding or diagnostic company partnerships could minimize the cost of high-sensitivity testing in resource-limited conditions[40]. Public health actions in LMICs can address cost and accessibility challenges by include HCV sensitivity testing. Combining HCV screening with HIV testing or other routine healthcare treatments could cut costs and increase screening rates. Using healthcare infrastructure and manpower, this integrated method could make HCV testing cheaper and more accessible in rural and underserved areas[39].

Due to cost, LMICs are unlikely to implement NAT-based HCV sensitivity testing. Many LMICs use less sensitive, cheaper RDTs since NAT's specialized equipment, trained workers, and logistical challenges make it difficult to adopt in decentralized healthcare systems. RDTs are easy and affordable, but their low sensitivity limits HCV diagnosis, especially early on. NAT cost reduction, RDT sensitivity enhancement, and point-of-care molecular tests are needed to screen LMICs accurately and solve global HCV care disparities. As these technologies advance, global health organizations, governments, and diagnostic companies must work together to diagnose HCV early and accurately[40].

9.2. False Positives and False Negatives

False positives and negatives in HCV sensitivity testing can affect patient therapy, public health, and screening. Bad test findings are common in diagnostic testing, but they complicate HCV care, since early and accurate diagnosis is essential for disease progression and transmission prevention. HCV false positives and negatives must be understood to enhance diagnosis and treatment[44]. Misdiagnosed HCV patients may have false negatives. Early identification is crucial for HCV treatment and cirrhosis and hepatocellular carcinoma prevention. If false-negative results delay diagnosis, the virus can damage the liver without treatment, raising the risk of serious health complications. In high-risk groups like intravenous drug users and unprotected sexual activity, false-negative results can spread the virus. Incorrect virus identification harms the person and the public health goal of limiting HCV spread[49].

Several factors induce HCV false-negatives. Test time versus infection stage is a crucial factor. ELISA, RDTs, and other HCV diagnostics detect immune system antibodies. The immune system takes weeks to produce antibodies after infection. A test during this interval may be negative despite HCV infection. Avoiding spreading and treating acute HCV infection requires early detection. Nucleic Acid Testing (NAT), which identifies viral RNA rather than antibodies, is better for early HCV diagnosis. However, NAT is not always available or cost-effective, especially in low-resource environments, increasing false negatives[50]. Immunity also creates false-negatives. HIV-positive and immunocompromised patients may not produce enough HCV antibodies. Poor immunological response can cause false-negative antibody-based tests. Low viral loads in antiviral patients may induce false negatives if the virus is below the test's detection threshold. More sensitive testing methods like NAT are needed to determine HCV infection. NAT accessibility is limited in many countries, making this problem difficult to remedy[59].

A false positive is when a test misidentifies someone as HCV-positive. Though less harmful than false negatives, false positives can have serious psychological and emotional impacts on patients. Positive HCV diagnoses are stressful due to long-term health issues and stigma in many societies. The aftermath of a false-positive diagnosis can create anxiety, depression, and fear. A false-positive diagnosis could ruin their personal and professional lives if they tell employers, insurance providers, or loved ones[57]. In addition to psychological trauma, false positives might cause unnecessary medical procedures. Positive results may require costly and time-consuming confirmation tests. People may receive unnecessary antiviral medicines, exposing them to side effects and treatment costs. While more sensitive confirmatory testing procedures like NAT may limit false positives, the patient may incur considerable emotional and financial harm. In resource-limited settings with insufficient confirmatory testing, patients may be doubtful about their diagnosis, increasing worry and uncertainty[52].

HCV testing false-positives have several causes. Main cause is cross-reactivity with other illnesses. People who have been exposed to HCV-like viruses or organisms may test positive for ELISA. Cross-reactivity can cause false-positive results in non-HCV-positive people. In unguided labs, incorrect sample handling or contamination can cause false-positive results. Low-quality tests or diagnostic kits may potentially give erroneous results in

areas with cheaper, less reliable testing[40]. HCV testing must be sensitive and specific to avoid false positives and negatives. A test's sensitivity and specificity determine its ability to detect infection and noninfection. Highly sensitive and specific testing eliminate false negatives and positives. For accurate HCV testing, technology must balance sensitivity and specificity. This balance can be difficult to achieve in resource-limited environments where advanced testing methods are expensive or scarce[48].

There are several ways to prevent HCV testing errors. Combining tests improves diagnosis accuracy. A screening test like ELISA or RDT can be confirmed by NAT or other sensitivity testing. Two-tiered testing lowers false positives and negatives by validating early results with a more accurate test. Technology and manufacturing can boost test sensitivity and specificity. More sensitive antibody, antigen, and point-of-care molecular testing is being developed to reduce false results[49]. Finally, HCV sensitivity testing false positives and negatives hinder patient therapy and public health. False negatives delay diagnosis and treatment, prolonging the infection and increasing transmission risk, while false positives cause stress and unnecessary medical treatments. These challenges can be addressed by improving testing sensitivity and specificity and offering reliable diagnostic tools in all healthcare settings. By minimizing false positives, HCV screening systems can enhance patient care and reduce the global burden of this chronic viral illness[50].

9.3. Accuracy and Reliability Concerns

HCV testing must be accurate and reliable to provide prompt and appropriate care. HCV sensitivity testing accuracy is affected by population diversity and false positives and negatives. To be effective, screening programs must address these difficulties, especially in resource-constrained settings. False positives and negatives complicate HCV diagnosis[33]. HCV testing in non-infected people may be false positives due to cross-reactivity or test processing errors. This outcome can lead to wasteful testing, patient distress, and healthcare expenses. The repercussions of false positives are substantial. Misdiagnosed HCV patients may worry about liver disease progression, social stigma, and transmission. In resource-limited settings, false positives necessitate more confirmatory testing, increasing healthcare expenditures. When a test fails to detect HCV in an infected person, false negatives can be worse. False negatives are especially problematic early in infection, when intervention works best[39]. False-negative results delay diagnosis and treatment, spreading the illness. A false negative can transfer HCV to high-risk groups including IV drug users and HIV co-infected patients. In antibody-based assays, the "window period" before antibodies become detectable produces false negatives. Nucleic Acid Testing (NAT), which directly detects viral RNA, is suggested for early detection but expensive[43].

Testing must be sensitive and specific to avoid false positives and negatives. Due to the limitations of antibody-based RDTs and ELISA, NAT is needed to prevent diagnostic errors. To avoid these sorts of errors, RDT and ELISA sensitivity and specificity are being improved and cost-effective point-of-care molecular diagnostics developed. Improved tests can minimize diagnostic uncertainty and speed up and accurate diagnosis[54]. Due to age, immunological state, and co-existing health concerns, HCV sensitivity tests differ by population. This makes it hard to get accurate test results across ethnicities. HIV and immunosuppressed patients may not produce HCV antibodies. Antibody-based assays like ELISA and RDTs may fail even if actively infected. Low-virus populations, such as those on antiviral treatment or early in infection, may have less sensitive immune response tests[58].

Age can affect test results. Immunological reactions that lower antibody levels can make antibody-based assays incorrect in older people. As liver regeneration slows with age, older people are more prone to develop significant liver disease soon. False-negative results may delay diagnosis for this group. Public health screening systems that don't account for test performance variations may overlook cases in particular populations, causing diagnostic and treatment gaps[61]. Some healthcare organizations use antibody tests followed by NAT for high-risk cases to address these concerns. This technique may not improve diagnosis accuracy in all cases due to cost and logistics. RDT and ELISA accuracy and dependability must be improved to ensure HCV screening programs in resource-limited settings deliver reliable results across demographic groupings[68].

9.4. Variability in Test Performance

Hepatitis C virus (HCV) tests differ in sensitivity and specificity by population. Test sensitivity detects HCV-positive people, while specificity detects HCV-negative ones. Diagnostic tests should be sensitive and specific to avoid false positives and negatives. However, age, immunological status, co-infection with other viruses (e.g., HIV), and population health can greatly affect screening assay results, making it challenging to attain population-wide test performance. HCV screening program consistency is problematic due to heterogeneity because one test may work well in one group but not another[53]. Age greatly affects HCV test findings. Age-related immunological responses to viruses like HCV affect diagnostic test sensitivity and specificity. A delayed and poorer immune response may cause elderly people to produce fewer HCV antibodies. Older people may receive false-negative HCV testing, especially early in infection when antibody generation is low. Delayed diagnosis and treatment in the elderly can harm health. Younger people, especially those with robust immune systems, may acquire more antibodies, making viral detection easier and boosting test results[51].

Liver function changes with age can affect HCV test results. Since their livers renew and repair less, older persons are more susceptible to HCV's long-term effects including cirrhosis and liver cancer. This makes diagnosis harder and promotes early detection. Due to antibody-based test limitations, elderly patients may require more sensitive procedures like Nucleic Acid Testing (NAT) to improve diagnosis[58]. Testing participants' immune health also influences performance. Cancer patients and organ transplant recipients on immunosuppressive treatment may not respond to HCV antibodies, resulting in false-negative testing. People with autoimmune diseases that inhibit antibody formation are also affected. NAT or other direct viral detection methods that do not rely on the immune system to detect HCV are recommended for these groups. Immunocompromised individuals can receive speedier treatment because NAT identifies viral RNA[59].

HIV co-infection affects HCV diagnostic test sensitivity and specificity. HIV co-infection is common in HCV-risk groups such IV drug users, complicating diagnosis. HIV suppresses HCV antibody production, increasing the probability of false-negative ELISA and RDT results. HIV-positive patients may not be diagnosed with HCV until late, missing out on treatment. HCV patients with HIV co-infection had faster liver disease development, making early identification critical[66]. Healthcare providers enhance HIV co-infection diagnosis in this population using NAT or other RNA-based tests. Without the antibody reaction, these tests directly detect HCV RNA, making them more accurate in weak immune systems. Co-infection rates are higher in low- and middle-income countries (LMICs), where cost and availability limit NAT implementation. Despite these drawbacks, antibody-based assays are still employed, leading to underdiagnosis or delayed diagnosis in co-infected patients[63].

Diverse HCV genetics increase test performance variability. World areas have different viral genotypes. Diagnostic testing may identify genotypes better depending on geography and population genetics, impacting test results. In frequent areas, genotype 1 tests may be sensitive and specific. Same test may perform poorly in regions with more genotypes 2, 3, or 4, resulting in more false negatives or ambiguous results. This heterogeneity highlights the need for regional HCV screening and diagnosis[33]. Test findings also depend on HCV infection stage. In acute sickness, standard testing may overlook antibody levels, resulting in false negatives. Conversely, persistent HCV patients have more detectable antibodies, improving test accuracy. Chronic HCV patients on antiviral treatment may have low viral levels, making identification challenging, especially with less sensitive tests. This indicates that the optimal test for accurate diagnosis depends on sickness stage[20].

Due to these challenges, standardizing HCV screening across groups is difficult. A one-size-fits-all strategy to HCV test performance is unlikely to work due to demographic and clinical differences. Instead, doctors must assess age, immunological state, co-infection, and regional HCV genotypes. These features might be addressed when creating HCV screening programs to improve diagnostic accuracy and timely care for HCV-risk people[57]. Developing sensitive and specific diagnostic methods that function across populations to overcome test performance variability. Point-of-care NAT and NGS may increase HCV testing accuracy. These methods can directly detect the virus's genetic material regardless of the patient's immune condition or co-infection, eliminating antibody-based diagnostics' limitations. These technologies are too expensive and difficult for wide application, especially in resource-limited areas[66].

HCV test performance variation makes screening programs across populations difficult to standardize. HCV genetic diversity, age, immunological condition, co-infection, and other viruses affect diagnostic assay sensitivity and specificity. To ensure accurate diagnosis and effective treatment, healthcare providers must consider these criteria while choosing diagnostic devices and screening programs. To overcome these challenges and improve HCV detection internationally, diagnostic technologies and sensitivity tests must be improved[55].

9.5. Standardization Across Diverse Populations

HCV sensitivity testing must be standardized for diverse groups to have reliable diagnosis. Demographics, immunology, and genetics affect HCV test results. Age, immunological state, co-infections, and regional HCV genetic variants must be standardized to ensure test sensitivity and specificity across demographic groups. HCV sensitivity testing accuracy depends on age and immunology. ELISA and RDTs may fail in older people due to diminished antibody production. Age-related variability can generate false-negative results, especially in newly infected persons without adequate antibody[36]. Delayed discovery is worse for older persons since HCV consequences like cirrhosis and liver cancer are more prevalent. NAT, which detects HCV RNA rather than antibodies, may be a better diagnostic approach but is costly and infrastructure-intensive. Immunity affects HCV tests. HIV-positive and immunosuppressed persons may not make enough antibodies, increasing false negatives in antibody-based diagnostics. It's crucial since HIV co-infection further damages HCV liver. These populations may need direct HCV detection methods like NAT to be diagnosed. The lack of NAT in low- and middle-income nations emphasizes the necessity for accurate, accessible immune-compromised diagnostics. Geographical HCV genotypes also hinder standardized testing. Some HCV genotypes are more prevalent in certain areas. Genotype 1 is widespread in North America and Europe, 3 and 4 in Asia and the Middle East.

Genotype can affect test performance since some tests are genotype-sensitive. Genotype-specific sensitivity can induce false negatives in rare genotypes, limiting HCV screening across regions[59].
To accommodate this variability, test makers must ensure diagnostic equipment can detect many HCV genotypes. Next-generation sequencing (NGS) may now uncover various genotypes and genetic variants that may affect sickness onset and treatment. Modern testing methods like NGS are expensive and need complex lab equipment, making them less accessible in resource-limited nations with different genotypes. Regionalizing HCV testing may ensure fair access to trustworthy diagnosis in healthcare systems. Genotype-specific tests in locations with high non-standard genotype prevalence or a combination of diagnostic methods may increase detection rates. Investing in point-of-care testing that can detect many HCV genotypes is essential for diverse and poor groups to receive effective HCV diagnosis. Personalized testing programs can improve global HCV morbidity and mortality reduction by being sensitive and specific across demographics[53].

10. Clinical Effectiveness

The clinical efficacy of HCV sensitivity testing is crucial to disease management. Clinicians can swiftly diagnose and treat HCV infections, improving patient outcomes. Early diagnosis lowers HCV-related liver complications such cirrhosis, liver cancer, and liver failure. HCV transmission is reduced by early detection and treatment, enhancing public health[42]. NAT has revolutionized HCV sensitivity testing. NAT detects HCV RNA earlier than antibody-based diagnostics, which depend on the host's immune response. Antibody testing takes up to 70 days to identify HCV, but NAT can detect it in 7 to 10 days. HCV infections can now be diagnosed and treated before liver damage due to this considerable window time reduction[30]. Early detection of acute infections by NAT improves patient outcomes. Acute HCV patients benefit from direct-acting antivirals. Due to sustained virologic response (SVR), these medications cure HCV by eliminating the virus from circulation. Earlier SVR prevents chronic HCV sequelae including cirrhosis and hepatocellular carcinoma, which cause significant morbidity and mortality. SVR early detection decreases the need for expensive and invasive liver transplants, making it a cost-effective healthcare strategy[36].
Early detection helps people and public health with HCV sensitivity testing. NAT and other sensitive testing methods reduce HCV transmission in high-risk populations such intravenous drug users, men who have sex with men, and prisons by discovering infections early. Undiagnosed acute or chronic HCV patients are more prone to transfer the virus through blood-to-blood contact. Healthcare providers can reduce transmission risk by training patients on safer injection practices or treating viral loads to undetectable levels after early identification[34]. HCV sensitivity testing must inform clinical decision-making to be effective. Accurate and early diagnosis helps doctors tailor treatment to each patient, improving outcomes. Acute HCV patients may need less antiviral treatment than persistent infections. Accurate diagnosis also identifies persons with severe liver disease or HIV co-infection who may benefit from rigorous treatment. To improve treatment outcomes and patient care, HCV infection stage must be precisely tested[47].
Early and accurate HCV diagnosis is needed due to effective direct-acting antivirals (DAAs). DAAs have improved HCV treatment with high cure rates, short treatment periods, and fewer side effects. DAA efficacy depends on timely dose. Patients diagnosed and treated early before liver damage respond better to DAAs and have higher SVR rates. DAAs may help people with severe liver disease like cirrhosis, although their treatment may be more complicated and require longer durations or other interventions. This highlights how crucial HCV sensitivity testing is for patient outcomes and treatment decisions[58]. Medical costs can be reduced by early HCV sensitivity testing. As severe cases require liver transplants, hospitalization, and long-term management of cirrhosis or liver cancer, chronic HCV infection is expensive. Early detection of HCV infections can reduce healthcare expenditures by preventing chronic liver damage. Early DAA treatment can cure the infection and prevent costly treatments, making it cost-effective. Preventing severe liver disease and its complications pays for sensitive diagnostic methods like NAT[1].
Early detection has shown clinical benefits, but sensitive HCV testing is difficult to obtain and implement. Low- and middle-income countries (LMICs) struggle to implement NAT owing to cost and infrastructure. These regions' healthcare systems may lack financial and laboratory resources to detect and treat NAT early. These patients may be diagnosed with HCV late, reducing treatment success and increasing liver disease burden[15]. HCV testing is being developed to be more easy and affordable while maintaining high sensitivity and specificity. Point-of-care molecular tests for HCV diagnosis without labs are being developed. These handheld devices identify and treat early in resource-poor areas. These changes could improve HCV screening programs worldwide by boosting access to sensitive testing methods, ensuring more people get early and accurate diagnoses regardless of location or healthcare resources[16].
Rapid Diagnostic Tests (RDTs) are increasingly used for HCV sensitivity testing as sensitivity and specificity improve. RDTs were less sensitive than NAT in early-stage infections, however successive generations have increased HCV antibody and antigen detection. These advances make RDTs valuable for scaling up HCV screening when NAT isn't feasible. Despite having poorer diagnostic accuracy than NAT, RDTs can detect chronic HCV patients and treat them, reducing the disease's effect. RDTs have clinical success because they

boost HCV testing in resource-limited settings, where early identification and treatment prevent illness[19]. HCV testing in public health initiatives has also enhanced sensitivity testing's clinical efficacy. Combining HCV screening with HIV or maternal health campaigns has increased diagnoses. This comprehensive approach helps doctors find HCV-risk patients who may not be screened. Integrated screening programs can increase HCV sensitivity testing to more patients utilizing current healthcare infrastructure, ensuring timely diagnosis and treatment[23].

HCV sensitivity testing clinical efficacy is essential for disease therapy and control. NAT can detect HCV infections early, allowing timely treatment to improve patient outcomes and reduce virus spread. Sensitive testing helps doctors optimize treatment, reduce HCV-related liver disease burden, and reduce advanced hepatic complications costs. While accessibility and cost difficulties remain, continued attempts to develop more affordable and accessible diagnostic techniques could expand HCV sensitivity testing worldwide, guaranteeing that everyone, regardless of location or socioeconomic position, can benefit from early diagnosis and treatment. As testing technology improves, HCV screening programs' clinical performance will be important to eliminating HCV as a public health problem worldwide[28].

10.1. Benefits of Early Detection and Treatment

Early HCV testing and treatment enhance patient outcomes, limit transmission, and lower healthcare costs. HCV is often diagnosed late, causing cirrhosis, liver cancer, and liver failure. Nucleic Acid Testing (NAT) can help healthcare providers diagnose and treat the infection early. Early infection therapy increases cure rates and reduces medical interventions. Most HCV patients can be cured by fast-acting DAA medications[11]. Early DAA treatment can cure HCV and prevent chronic complications with a sustained virologic response. This SVR greatly minimizes liver damage risk, improving patient quality of life and longevity. Intravenous drug users, healthcare workers, and those without healthcare benefit from early treatment, which lowers HCV transmission. Early diagnosis helps healthcare personnel educate patients on transmission prevention and start treatment immediately, decreasing community spread[17].

Early detection and treatment save expensive, long-term HCV treatment. Chronic HCV often necessitates liver transplants, cirrhosis hospitalizations, and liver cancer treatment. Treating the virus before it affects the liver saves healthcare systems money. Early diagnosis and treatment lessen daily disruptions and may prevent severe liver illness-related job interruption and productivity loss. HCV patients can be reassured of early treatment's high success rate, minimizing social and psychological strain[30]. Fast liver damage diagnosis and treatment improve mental and emotional wellness by reducing anxiety and speeding recovery. Early detection and treatment reduce HCV transmission and improve public health. Early HCV testing and treatment improve results, reduce transmission, and lower healthcare costs. These benefits can be maximized by encouraging early diagnosis and treatment, especially in high-risk populations and high-prevalence areas. These programs pursue individual and public health goals to eliminate HCV, a major public health issue[49].

10.2. Integration into Public Health Programs

HCV screening and treatment must be integrated into public health programs to target underprivileged areas, limit transmission, and enhance management. High-prevalence areas and high-risk groups including injector harm reduction programs, mother-child health programs, and HIV treatment providers should screen for HCV. Integrating HCV testing into existing services can reach underserved patients[42]. This complete approach normalizes HCV testing, lowers stigma, and simplifies it for sensitive populations. HIV/TB programs can test for HCV to address overlapping risk factors that create high co-infection rates. Many HIV/TB patients are at risk for HCV due to intravenous drug use or unsterile medical procedures. HCV testing with HIV or TB medicines helps doctors find and treat co-infections, improving patient care. In resource-constrained environments, integrated programs speed up service delivery and allow doctors to treat several illnesses[38].

Jail inmates, injectors, and vulnerable communities with limited healthcare access benefit from HCV public health programs. Many of these communities avoid HCV testing and treatment due to stigma, discrimination, and transportation concerns. These patients can receive HCV testing through mobile health clinics, harm reduction programs, or community services. HCV testing and education remove myths and encourage at-risk individuals to get tested and treated. The use of HCV testing in public health can optimize resource use and reduce redundancy[18]. Instead of launching new HCV programs, hospitals can use existing resources and infrastructure to increase testing coverage. This cheaper technology can extend HCV testing in low- and middle-income countries (LMICs) with limited healthcare spending without overburdening healthcare facilities. HCV screening as part of routine medical visits, primary care, and other community health programs improves early detection and treatment[15]. Finally, comprehensive HCV screening and therapy diminish liver disease and chronic HCV effects. By diagnosing and treating more people, these efforts reduce HCV mortality. Public health integration is a good method to meet the WHO's 2030 HCV elimination objective. Integrating HCV testing programs improves community health, healthcare access, equity, and public health efforts to fight infectious diseases[23].

Table 1: Summary of HCV Sensitivity Testing Methods: Innovations, Advantages, Limitations, and Clinical Effectiveness

Testing Method	Innovation	Advantages	Limitations	Clinical Effectiveness
Nucleic Acid Testing (NAT)	Direct detection of HCV RNA, reducing window period to 7–10 days	High sensitivity and early detection, useful in high-risk cases	High cost, requires complex lab infrastructure, limited accessibility in LMICs	Very effective for detecting early-stage infections, reducing transmission in blood banks and transplant screenings
Rapid Diagnostic Tests (RDTs)	Simple and quick test to detect HCV antibodies or antigens	Cost-effective, rapid results, useful in resource-limited settings	Lower sensitivity in early infection, risk of false positives/negatives	Accessible for large-scale screenings; effective for chronic infections, not ideal for recent infections
Enzyme-Linked Immunosorbent Assay (ELISA)	High-throughput screening for HCV antibodies	Low cost, scalable for large-volume testing, high specificity	Limited early detection due to delayed antibody production	Useful for identifying chronic infections; commonly used in moderate to high prevalence areas
Next-Generation Sequencing (NGS)	Comprehensive HCV genome analysis, detects genetic variations	Detects multiple genotypes, useful for understanding treatment resistance	High cost, requires advanced lab infrastructure and expertise	Effective for tailoring treatment and managing complex cases, less accessible for routine screening
Dual-Detection RDTs	Detects both HCV antibodies and antigens on one strip	Improved accuracy in early infection detection, still affordable	Slightly higher cost than standard RDTs, not as sensitive as NAT	Increases accessibility of early detection in resource-limited areas, can aid in rapid screening

11. CONCLUSION

Recent advancements in HCV sensitivity testing have revolutionized the diagnosis, management, and containment of this global health burden. Techniques such as nucleic acid testing (NAT), rapid diagnostic tests (RDTs), and next-generation sequencing (NGS) have made HCV diagnosis faster, more accurate, and widely accessible. NAT, considered the gold standard in high-resource settings, detects HCV RNA before antibody production, enabling early diagnosis and treatment while preventing transmission. However, its high cost and infrastructure demands limit its application in low- and middle-income countries (LMICs), where HCV prevalence is highest.To address these challenges, point-of-care molecular tests and enhanced RDTs have emerged as more affordable alternatives. While RDTs are less sensitive than NAT, advances in dual-detection methods for antibodies and antigens have enabled large-scale screening in remote areas. Nonetheless, RDTs struggle with early-stage infections and require confirmation testing for accuracy. Factors such as age, immune status, HIV co-infection, and HCV genetic variability further complicate diagnostic sensitivity and standardization, emphasizing the need for tailored approaches to diverse populations.

The lack of infrastructure and high costs in LMICs delay diagnosis, reducing treatment effectiveness and increasing transmission. Integrating HCV screening with existing healthcare services, such as HIV or maternal health programs, has proven effective in reaching underserved populations and improving cost efficiency. Such integrated approaches leverage existing resources, expanding diagnostic coverage in resource-limited settings.Eliminating HCV as a global health issue requires continued innovation, funding, and collaboration. Researchers must develop affordable, sensitive, and population-specific diagnostic tools, while policymakers must enhance healthcare infrastructure and access to advanced technologies. Emerging innovations, including AI and molecular diagnostics, hold promise for achieving the WHO's 2030 goal of eradicating viral hepatitis. Sustained investment and global efforts are critical to reducing HCV-related morbidity and mortality worldwide.

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