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Cost-Effectiveness Analysis of Rapid Test Compared to Polymerase Chain Reaction (PCR) in Patients with Acute Respiratory Syndrome

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Abstract

Background: It is important to have a rapid and cost-effective laboratory test for the early diagnosis of respiratory diseases.The aim of this study was to analyze the cost-effectiveness of rapid tests and PCR in patients with suspected influenza.

Methods: This study was a cost-effectiveness analysis from a community perspective that in which patients who were referred to the emergency department of selected hospitals of IUMS university with suspected respiratory symptoms of influenza were studied by convenience sampling method. The intervention and comparator were rapid tests and PCR respectively.effectiveness indicators in this study include sensitivity, specificity, positive and negative predictive value of both tests, and it examines costs from a community perspective.After drawing the decision tree model in the TreeAge software, the incremental cost-effectiveness ratio was calculated and to evaluate the strength of the analysis results, one-way and two-way sensitivity analyses on all cost and effectiveness parameters were used.

Results: According to the findings of this study, the effectiveness index in rapid test and PCR is equal to 0.90 and 0.91, respectively, and the average cost of the two tests is equal to 62.157 and 201.37$, respectively, the ICERwas 25450.27 and the cost-effectiveness threshold was estimated equal to 6000 according to the per capita GDP of the country. One-way and two-way sensitivity analysis showed that the result of cost-effectiveness analysis did not change, and the rapid test is cost-effective.

Conclusion: Rapid test is less costly and effective than PCR, but the cost difference is greater than the difference in effectiveness and in terms of effectiveness indicators, both diagnostic tests are almost similar, and this cost difference has led to the choice of the rapid test as a cost-effective option. Therefore, it is recommended that physicians prioritize rapid tests in the diagnosis of respiratory diseases.

Keywords: Cost-Effectiveness, Rapid Test, PCR, Respiratory Infections

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Introduction

Acute Respiratory Distress Syndrome (ARDS) is a rapidly progressing disease that first presents with shortness of breath, tachypnea, and hypoxemia and then progresses rapidly to respiratory failure. Influenza is a highly contagious and acute viral disease of the respiratory tract that causes the most damage to the lower res piratory tract (1). The virus of this disease belongs to the Orthomyxoviridae that are coated with single-stranded RNA genome and

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↑What is "already known" in this topic:
Determining an efficient diagnostic method with the lowest cost and with the highest accuracy is one of the most important concerns of health professionals and patients with acute respiratory symptoms and suspected influenza referred to the emergency departments.

→What this article adds:
This study may have significant policy and clinical implications for health policymakers, laboratory specialists, emergency medicine specialists, and health managers.

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negative polarity and in fragments (2).

It is estimated that worldwide outbreaks of influenza virus cause 3-5 million severe illnesses and 350-250 thousand deaths annually, and the economic impact of influenza outbreaks and economic costs of $ 10-60 million per million populations in industrialized countries (3). In the US, the total annual economic burden of seasonal influenza has been estimated at $11.2 billion, of which $8.0 billion were indirect costs. Similarly, in Europe, the total costs of influenza may range from €6 to €14 billion per year (4). Prompt detection prevents the spread and control of infection and prevents further economic losses (2). Also, the impact of this disease and other acute respiratory infections on productivity and use of health care resources is very high, and the highest rates of disease and mortality are seen primarily in the elderly and those with underlying respiratory disease (5).Therefore, rapid diagnosis of influenza is not only necessary for early treatment and prevention of virus transmission but also for the management of scarce economic resources (6).

One of the tests used to diagnose this disease is Rapid Influenza Diagnostic Tests (RIDTs), which are capable of detecting viral nucleoproteins and, based on scientific evidence, including their properties, 92% specificity and results in the shortest time is the rapid detection of influenza infection is very important. Therefore, rapid diagnosis methods play a major role in controlling various disease epidemics. So that the whole process of diagnosing the cause of the disease can be done in one working day (7, 8). Another test is Polymerase Chain Reaction(PCR), which is based on copying the DNA or RNA sequence of the sample and based on this can diagnose various diseases, including acute respiratory diseases (9).

Previous studies have shown that reducing the length of hospital stay, use of antibiotics and use of laboratory facilities are very cost-effective for patients with influenza virus, parainfluenza virus, and adenovirus infection after the rapid test (10-12). Also, in the study of Cheerer et al., routine use of PCR may not be appropriate due to its high cost, especially if PCR is used alone and in their study, the importance of clinical tools and cost-effectiveness analysis for these trials for better decision-making is emphasized (13). Therefore, determining an efficient diagnostic method with the lowest cost and with the highest accuracy is one of the most important concerns of health professionals. In this regard, diagnostic studies with comparative design are of special importance in which the reliability or validity of a test in different ways is examined (14-16).

Cost-effectiveness analysis of medical care is a major concern worldwide, and therefore evaluating the clinical and economic impact of all clinical measures and interventions has great importance (17, 18). Therefore, due to the limitations in terms of human resources and laboratory and medical facilities, including hospitalization costs, traffic in emergency rooms during the flu season and the unnecessary use of broad-spectrum antibiotics experimentally and doubts about starting antiviral treatment this study designed to compare rapid test with the standard method (PCR) in patients referred to the emergency department of selected hospitals in terms of cost and effectiveness.

Methods

This descriptive-analytical cross-sectional study was designed for cost-effectiveness analysis. In this study, was used the decision analysis model (decision-tree model) and cost-effectiveness of influenza rapid test compared to the standard method (PCR) in patients with suspected influenza was investigated. The criteria for calculating the costs were from the community perspective, including direct and indirect costs of diagnosis. The data were extracted directly from the records of patients as well as interviews by following the process of diagnosis until a definite result was obtained. The effectiveness indicators that were studied in this model were: sensitivity, specificity, positive and negative predictive value of the studied tests.

In this study, patients who were referred to the emergency department of RasoolAkram and Firoozgar hospitals with suspected respiratory symptoms were considered as a sample in the infant age range up to 90 years (with an average age of 54 years). In this study, no restrictions were considered for the selection of patients, and in all of them, after clinical examinations and taking a history and receiving demographic information, a prepared sample was performed from nasal lavage or swabs removed by rapid and gold standard test methods (virus antigen determination).

Rapid test along with PCR was used to collect data. The rapid test kit used in this study was Quick Navi–Flue A and B, which was examined after sampling, and during the first 5 minutes, if a positive result was observed, the rapid test result was reported and if no positive result was observed it was re-examined at 5-minute intervals to evaluate and report the positive and negative results more carefully. Quick Navi-Flu is an immunochromatography-based rapid diagnostic test with originally developed mouse monoclonal influenza virus-specific antibodies (19). The PCR result was reported between 2-10 days after sending the samples to the health reference laboratory, and in some cases, the final report result lasted more than 10 days. The results of other studies were used to evaluate the sensitivity, specificity, positive and negative predictive value of the gold standard.

In this study, for cost-effectiveness analysis, after drawing the decision tree model in the TreeAge pro 2011 software, the ICER was calculated and the WHO approach was used to calculate the cost-effectiveness threshold so that if the incremental cost-effectiveness ratio is less than three times the GDP per capita, the strategy is cost-effective (20, 21). An ICER is calculated by dividing the difference in total costs (incremental cost) by the difference in the chosen measure of health outcome (incremental effect) (18, 22).

One-way and two-way sensitivity analysis were performed to increase the accuracy and validity of the results , considering that the One-way sensitivity analysis specifies the effect of changing a parameter on the results within a specified range. Thus, it is necessary to evaluate the simultaneous effect of two parameters in the model in order to increase the accuracy of the results and the generalizability of the research findings accordingly, the Two-way sensitivity analysis was used for this purpose (23,

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24).

Results

Basic patient information

In this study, the mean age of the patients was 54 years, of which 60.2% were male and 39.8% were female. Also, in terms of the history of underlying disease, 66 (58.4%) patients had no history of any underlying disease. 12 patients had a history of diabetes (10.6%) and 12 patients had lung disease (10.6%), 13 patients had more than one underlying disease, with the highest number being related to 5 (4.4%) patients with heart disease and lung and 3 (2.7%) were diabetic and pulmonary also in terms of the most important symptoms of the disease, in 22 patients Coryza (19.5%), 36 patients had body pain(31.9%) and 48 patients had a fever (42.5%) (Table 1).

Table 1. Basic patient information

characteristic		Frequency (%)
Age average		54
Gender (Male)		68 (60.2)
History of underlying disease		
	No history of underlying disease	66 (58.4)
	Diabetes	12 (10.6)
	Lung disease	12 (10.6)
	Heart and lung diseases	5 (4.4)
	Diabetes and lung diseases	3 (2.7)
Symptoms		
	Fever	48 (42.5)
	body pain	36 (31.9)
	Coryza	22 (19.5)

Table 2. Profile of diagnostic tests

Specifications of tests / type of tests	Rapid test	PCR (reference)
Sensitivity (%)	78	84 (25)
Specificity	100	96.5 (25)
Positive predictive value (%)	100	98 (26)
Negative predictive value (%)	98	80 (26)
Total costs ($)	62.157	201.37

Cost-effectiveness analysis

Cost-effectiveness model: Figure 1 shows the cost-effectiveness model for patients with respiratory infections.

As shown in Figure 1, patients enter different conditions by performing diagnostic tests for influenza, which include isolation, non-isolation, and antiviral treatments.

Cost-effectiveness: The effectiveness of the PCR test in patients with respiratory infections is 0.91 and this index of effectiveness in the rapid test is 0.90. Also, the cost of PCR test in these patients is equal to 201.37 $ and in the rapid test is equal to 62.157 $. Therefore, the PCR test has more cost and effectiveness than the rapid test and the amount of incremental cost is equal to 139.213 $ and the amount of incremental effectiveness is equal to 0.00547 which is very small. Also, theICER of the two diagnostic methods is 25450.27422 and the average cost-effectiveness for PCR is 220.86 and for a rapid test is 68.58476.Therefore, considering the cost-effectiveness threshold and the average cost-effectiveness of the two interventions, rapid test compared to PCR is cost-effective (Tables 2 and 3 and Fig. 2).

Sensitivity analysis

Accordingly, all parameters related to the cost and effectiveness of disease diagnosis methods were selected for sensitivity analysis using the tornado diagram. According to this graph, the specificity PCR test had the greatest impact on the analysis result and the variables of rapid test sensitivity and PCR sensitivity were the most influential in the second and third rows, respectively.Based on one-way sensitivity analysis, by changing the characteristic parameter of PCR test in a certain range (2%), from

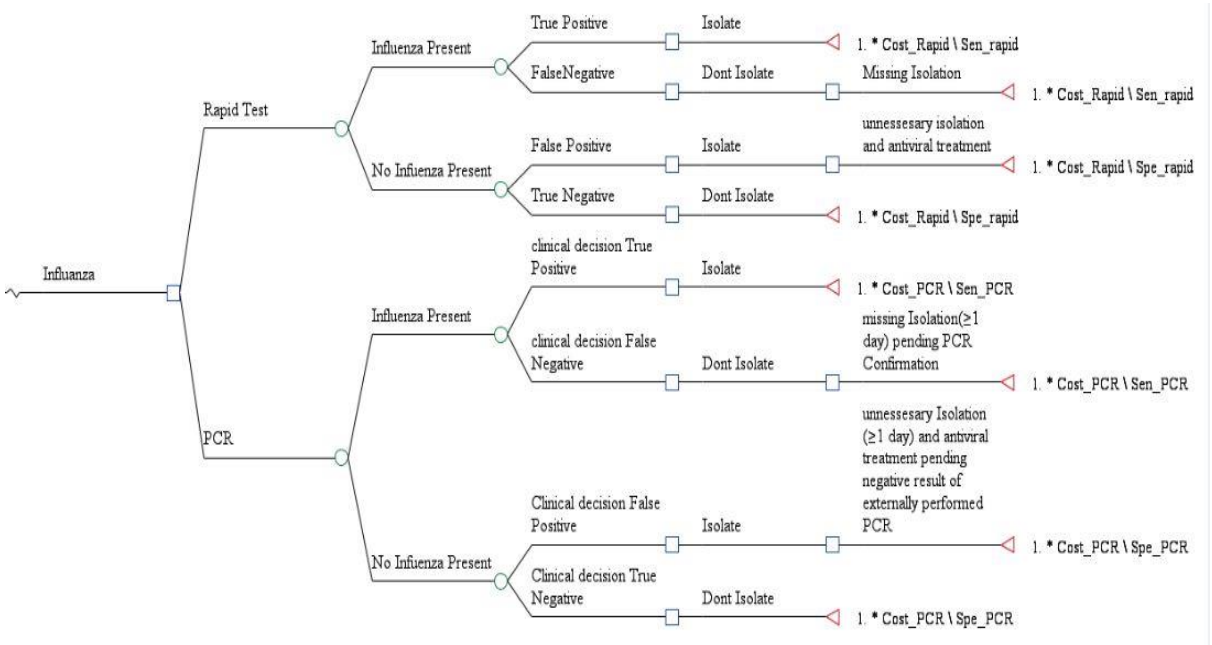

Fig. 1. Decision tree model for diagnostic tests

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Table 3. Cost-effectiveness of diagnostic tests

inter	Eff	Cost	Marginal value	IncrEff	IncrCost	IncrCE	AvgCE
PCR	0.91175	201.37	25450.27422	0.00547	139.213	25450.27422	220.86
Rapid Test	0.90628	62.157	0	0	0	0	68.58476

Inter: intervention, eff: effectiveness, incrEff: incremental effectiveness, incrCos: incremental cost, incrCE: incremental cost-effectiveness, avgCE: average cost-effectiveness

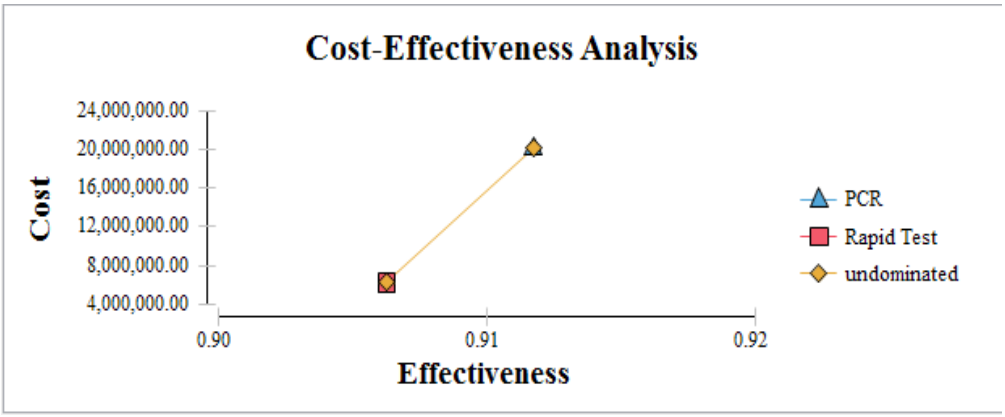

Fig. 2. Graph the cost-effectiveness of diagnostic tests

0.9457 to 0.965, PCR test is dominated and the rapid test is cost-effective and in the range of change from 0.97465 to 0.9843 PCR test is cost-effective. Also, based on the results of two-way sensitivity analysis, the parameters of PCR specificity and rapid test sensitivity were selected and their amount was changed to ±5% for sensitivity and ±2% for the specificity of baseline and was observed by changing the parameters in a certain range in a wide range, the rapid test is cost-effective compared to PCR (Table 4, Figs. 3 and 4).

Discussion

Influenza is a severe, contagious, and acute viral disease of the respiratory system that is on the list of diseases cared for by the World Health Organization. This disease can cause major economic and social damages and morbidity and mortality, especially in children and the elderly.

Table 4. Sensitivity analysis results

Parameter	Base value	Range of sensitivity analysis	CE range of rapid test	CE range of PCR
One-way sensitivity analysis				
PCR Specificity	96.5	0.945-0.984	0.945-0.974	0.974-0.984
Two-way sensitivity analysis				
PCR Specificity	96.5	0.945-0.984	0.945-0.984	0.966-0.984
Rapid test sensitivity	78	0.741-0.819	0.741-0.819	0.741-0.764

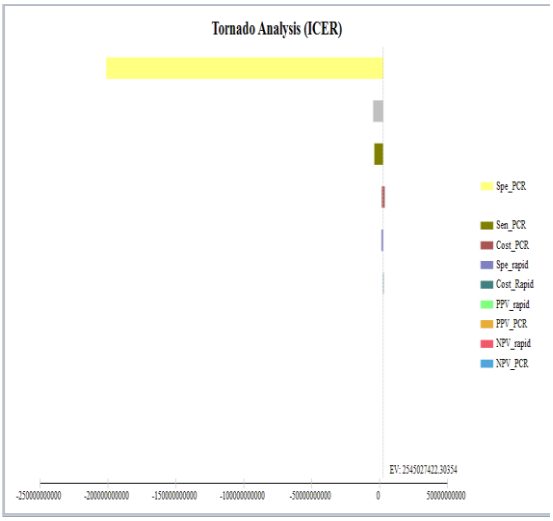

Fig. 3. Tornado model

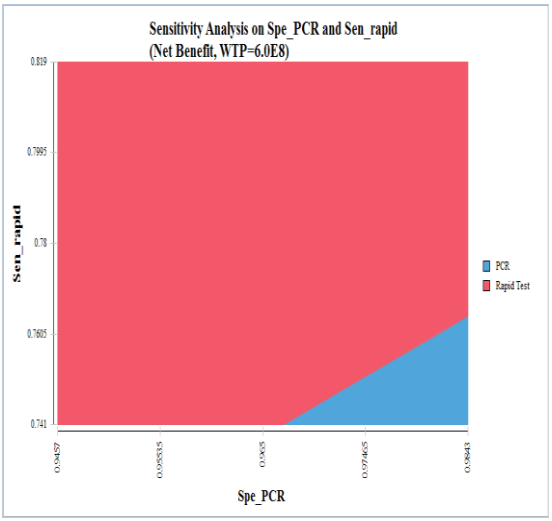

Fig. 4. Two-way sensitivity analysis

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Occupying hospital beds and increasing the number of patients in emergency rooms during an outbreak are other problems facing the health system (27-29).

The use of Point-of-care testing (POCT) for accurate and rapid diagnosis of influenza in an outpatient setting is highly desirable for initiating early and effective antiviral therapy. Early detection of influenza and timely initiation of antiviral therapy at the peak of the flu season and other respiratory infectious diseases is very important (30, 31). To date, little research has been done on the economic benefits of rapid tests and some aspects of resource management during inpatient rooms, as well as on its cost-effectiveness with the approach of effectiveness indicators such as sensitivity, specificity, positive and negative predictive value, not much research has been done.

In this study, we used a decision analysis model to evaluate the cost and effectiveness of two strategies for diagnosing respiratory virus infections.According to the results of this study, the average cost of rapid tests in patients is equal to 62.157 $ and this cost for people who have PCR tests is equal to 201.37 $. Also, the effectiveness index in this study is 0.90 for rapid test and 0.91 for PCR.In addition, the sensitivity, specificity, positive and negative predictive values of rapid test are 78, 100, 100 and 98%, respectively, and these indices for PCR are 84, 96.5, 98 and 80%, respectively.Based on the Akashi study, Quick Navi-Flu is more sensitive than GOLD SIGN FLU to diagnosing patients with influenza A and B. (19). The results are not consistent with our study, which can be due to the sample under study and the research method of their research with the present study.Another study conducted at the Centers for Disease Control and Prevention by Faix et al. was reported that the sensitivity of rapid influenza test was 40-69% (10). In a study conducted by ShawanVasoo et al. (2009) to compare three types of influenza rapid tests, the sensitivity of the tests was reported to be between 46.7 to 53.3% (32). In comparison with the results of the present study, the sensitivity of the rapid test was higher in our study.

In this study, we concluded that PCR test was more cost-effective than rapid test, and according to the cost-effectiveness threshold and the average cost-effectiveness of the two interventions, the rapid test is more cost-effective than PCR and to determine the strength of the study results, sensitivity analysis was performed on cost and effectiveness parameters, and it was observed that the results of the analysis did not change much and the rapid test was cost-effective compared to PCR. Gonzalez stated in his study that using RIDT to help diagnose H1N1 influenza increases the certainty and reliability of the diagnosis and reduces the average cost per suspected and infected patient (33). Also, according to a study by Diel., The use of the Solana® test as an example for a new generation of influenza rapid tests reduces the overall cost of suspected cases of influenza in the emergency department of a German hospital, as well as the routine use of these rapid tests can have a direct and positive effect on influenza control (6). The Soto study showed that the use of rapid PCR test saves money by reducing the use of resources such as laboratory tests and technical staff, disposable equipment, as well as by increasing the productivity of health care personnel in the examination room and emergency quarantine room saves costs (34). The findings of the You et al. study also showed that the use of rapid PCR could be a cost-effective option in the early detection and diagnosis of influenza (31). The study by Scherer et al. concluded that routine use of PCR might be difficult due to its high cost, especially if PCR is used alone, and their study emphasizes the importance of clinical tools and cost-effectiveness analysis as a better reason for the decision (13). All these studies are consistent with the results of our study. Also, according to the results of a study by Rajalahati et al., routine use of polymerase chain reaction test for all samples of patients with suspected respiratory infections in a low-prevalence environment is not cost-effective, and if PCR is performed only on true positive samples, that option will be the dominant strategy, that is, it will be a cost-effective item in making the right decision to treat and isolate patients (35).

Based on a study by Mahoney et al., It was concluded that the use of PCR is the least expensive strategy for diagnosing respiratory viral infections in children and creates significant savings for hospitals (36). Also, based on the study of Timbrook et al., It was concluded that performing a rapid diagnostic test with the diagnosis of genotypic resistance may lead to additional costs but can be an optimal way to increase the quality of life of patients with Enterobacteriasis (37). The reason for the inconsistency of the results was the study of other diseases, and the sample under study was different from our study.

Also, by interpreting the results of the present study, it can be said that the key to reducing costs in hospital emergency rooms for influenza tests is in the time interval between taking a swab in the emergency room and receiving the test results. It is sent out of the hospital and the report of the test result, which is mainly a PCR diagnostic test, arrives at the hospital one or two days later. During this time, patients need antibiotics and increased hospital costs. On the other hand, every time a person is misdiagnosed as a patient, hospital beds are occupied and the capacity of the hospital is reduced, which leads to a decrease in hospital income. Other studies have also reported that using rapid tests reduces the use of antibiotics in hospitalized adults or in children with pediatric emergencies (38, 39). Wu et al. Also concluded in their study that performing a rapid test reduces the length of hospital stay by 1.3 days. Also, by taking this test, the consumption of antibiotics in the hospital is significantly reduced and reduces costs by $ 391,000 per year (40). Another similar study was conducted by Brachmann et al., concluded that by testing 812 suspected influenza patients using the Alere® Influenza A&B test during the outbreak season, a total of 2,733 hours could be saved and this time will be more than enough hours to spend the space of an additional room in the emergency department, so this room can be used for other tasks (41). And the study done by Dugas et al. stated that the economic benefits of using rapid influenza test for emergency department patients at risk for influenza-related complications depend on factors such as influenza prevalence, physician-based treatment, or rapid

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test, and treatment of all patients are more effective and less costly than no treatment (42).

The present study faces the inherent limitations of the decision analysis model that the results of the model are exposed to uncertainty from the model inputs. Therefeore, sensitivity analysis was performed on key parameters. It is recommended that studies be performed on the cost-effectiveness of rapid test and PCR in Covid-19 patients.

Conclusion

The results of our study showed that performing a rapid test is less costly and effective than PCR, but the cost difference is greater than the effectiveness difference, and in terms of effectiveness indices, both diagnostic tests are almost similar, which makes the difference in cost and rapid test should be selected as a cost-effective option.

Acknowledgment

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Conflict of Interests

The authors declare that they have no competing interests.

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