Serum microRNA-29a and microRNA-361-5p as Potential Diagnostic Biomarkers for Active Pulmonary Tuberculosis

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ABSTRACT

Background: Tuberculosis (TB) remains a major global health problem. More effective biomarkers for use in TB diagnosis, prevention, and treatment, are urgently needed. We aimed to detect expression of microRNA (miR)-29a and miR-361-5p in sera of patients with active pulmonary TB, attempting to evaluate their role as potential biomarkers for the early diagnosis of pulmonary TB infection. Subject and methods: using real-time PCR (RT-PCR), relative expression levels of miR-29a and 361-5p were analyzed in serum samples from patients with active pulmonary TB (n=20), patients with pulmonary infection caused by bacteria other than M. tuberculosis (n=15), and healthy subjects (n=15). The receiver operating characteristic (ROC) curve was used to evaluate the diagnostic effect of each miRNA. Results: We found the expression of serum miR-29a was significantly elevated in TB infected patients compared to other bacterial infection group and healthy subjects (P<0.01). On the other hand, there was no significant difference of miR-361-5p expression (P=0.05). MiR-29a exhibited a good distinguishing efficiency in discriminating the TB infected group from the control groups, but miR-361-5p exhibited a poor distinguishing efficiency. Conclusions: The present study demonstrated that the expression of miR-29a in serum was highly significantly elevated in TB infected patients. The diagnostic performance of miR-29a is better than miR-361-5p for pulmonary TB. We recommend large scale studies to investigate the molecular role of both miRNAs in TB infection. Also, further studies are needed to assess the diagnostic efficiency of miR-29a as a biomarker for different situations including protection by vaccination, discrimination of latent and active disease, assessment of treatment outcome, and relapse risk.

Key words: Tuberculosis (TB), MicroRNAs (miRNAs), miR-29a, miR-361-5p, Real-time polymerase chain reaction (RT-PCR).

INTRODUCTION

Tuberculosis (TB) remains a major global health problem, causes morbidity among millions of people each year and ranks as the second leading cause of death from an infectious disease worldwide (1). The latest estimates that there were 8.6 million new TB cases and 1.3 million TB deaths in 2012 (2). Early diagnosis is essential for effective TB control and therapy. Current diagnostic approaches rely on the detection of the pathogen in clinical specimens. However, due to the heterogeneous clinical presentations of M. tuberculosis infection (active TB disease/asymptomatic latent TB infection; pulmonary and/or extrapulmonary TB), the development of affordable diagnostic tests based on host biomarkers is urgent in order to improve the quality of the TB diagnostic process in paucibacillary or not microbiologically confirmed cases (e.g. children, HIV-positive individuals, extrapulmonary cases) (3).

MicroRNAs (miRNAs) are small, non-coding RNAs approximately 21 nucleotides in length. They modulate gene function at the post-transcriptional level and act in fine tuning various processes such as development, proliferation, cell signaling, and apoptosis (4). MiRNAs have been found in tissues and also in serum and plasma, and other body fluids, in a stable form that is protected from endogenous RNase activity. The potential for the use of these circulating miRNAs as biomarkers of disease and as targets of therapeutics is promising for various diseases especially cancer (5). Recently several research groups have reported studies on miRNAs involved in TB to provide diagnostic biomarkers and new avenues for studying the immune response. Multiple microarrays have been performed on samples derived from TB patients, ranging from peripheral blood mononuclear cells (PBMCs) (6-7), pleural fluid mononuclear cells (8), pooled serum (9, 10), sputum (11), and even PBMCs stimulated with mycobacteria or mycobacterial ligands ex vivo (12). In addition to expression...
analysis, microRNA single nucleotide polymorphism (SNP) analysis has revealed a correlation between pulmonary tuberculosis and SNPs within the corresponding miRNAs(13). Steiner et al.(14) identified miRNA (miR)-29 as a central non-redundant suppressor of IFNγ and increased miR-29 expression promoted susceptibility against mycobacterial infections(15). Recently it was demonstrated that miR-361-5p was relatively abundant in bleomycin-induced fibrosis in mouse lungs and that its potential target genes may contribute to the understanding of the molecular mechanisms of lung injury and fibrosis(16). 361-5p target SP-1 transcription factor (SP1) that was a key signaling pathway for IL-10 expression in the lung(17).

Based on this information, we aimed to detect expression of miR-29a and miR-361-5p in sera of patients with active pulmonary TB, attempting to evaluate their role as potential biomarkers for the early diagnosis of pulmonary TB infection.

SUBJECTS & METHODS

Subjects

The current study was conducted on 50 individuals; divided into three groups. Group I: included 20 patients with active pulmonary TB, selected from the Chest hospital, Abbasyia, Cairo in the period from November 2012 to February 2013. Patients were diagnosed on the basis of positive results of sputum smear and TB culture, in combination with clinical symptoms and a chest X-ray examination. Peripheral venous blood was drawn from the patients prior to initiation of anti-TB treatment. Patients were excluded if they had a history of diabetes, cancer or coinfection with other pathogens, such as HIV, HBV, or HCV.

Group II: included 15 patients selected from the Chest department, Ain Shams University Hospital in the period from February to March 2013. Patients were diagnosed on the basis of positive results of sputum smear and TB culture, in combination with clinical symptoms and a chest X-ray examination. Peripheral venous blood was drawn from the patients prior to initiation of anti-TB treatment. Patients were excluded if they had a history of diabetes, cancer or coinfection with other pathogens, such as HIV, HBV, or HCV.

Group III: included 15 healthy age- and sex-matched individuals recruited as normal controls. Tuberculin skin test (TST) was performed to exclude latent TB infection (LTBI) from healthy controls. They were free of any clinical symptoms of any infectious disease. Informed consent was obtained from all the subjects enrolled in this study.

Methods

Sample collection:

Five milliliters of venous blood were collected from each participant in the studied groups. Samples were centrifuged at 3,000 rpm for 10 min, and the serum was removed, aliquoted, and stored immediately in −80°C until analysis. Relative expression of miR-29a and miR-361-5p in the collected samples involved the following steps: miRNA extraction, reverse transcription, and real time PCR.

(1)RNA Extraction:

Total miRNA was extracted using miRn easy Serum/Plasma Kit (cat.no.217184, Qiagen, Hilden, Germany) following the manufacturer’s protocol. The miRn easy Serum/Plasma Kit combines phenol/guanidine-based lysis of samples and silica-membrane–based purification of total RNA. QIAzol lysis reagent, included in the kit, is a monophasic solution of phenol and guanidine thiocyanate, designed to facilitate lysis, to denature protein complexes and RNases, and also to remove most of the residual DNA and proteins from the lysate by organic extraction. The purified miRNA sample was stored at -80°C till further analysis.

(II) Reverse transcription:

Extracted total miRNA was reverse transcribed to cDNA by miScript IIRT Kit (cat.no.218161,Qiagen, Hilden, Germany) following the manufacturer’s protocol using miScript HiSpec Buffer. The undiluted cDNA were stored at a –20ºC freezer till real-time PCR.

(III) Real time PCR (RT-PCR):

Relative expression levels for the 2 candidate miRNAs (miR-29a and miR-361-5p) were analyzed in relation to the housekeeping miRNA SNORD68-11 by a miRNA-specific miScript Primer Assay and the miScript SYBR Green PCR Kit (Qiagen, Germany). All samples were analyzed following the manufacturer’s protocol, using the Rotor Gene RT-PCR detection system (Qiagen, Germany). The reaction mix was prepared for a volume 22 µl per well reaction volume as following: 12.5 µl of 2x QuantiTect SYBR Green PCR Master Mix, 2.5 µl 10x miScript Universal Primer, 2.5 µl 10x miScript Primer Assay and 4.5 RNase-free water. The reaction mix was mixed thoroughly but gently, and dispersed appropriate volumes into the rotor-disc wells then 3 µl template cDNA was added, to reach 25 µl as final volume. Carefully, tightly the disc was sealed with rotor-disc heat-sealing film. The real-time cycler was programmed as: initial activation step 15 min 95°C for HotStarTaq
DNA Polymerase activation. Three-step cycling: denaturation 15 sec 94ºC, annealing 30 sec 55ºC, extension 30 sec 70ºC, for 40 cycles. The cycle threshold (CT) is defined as the number of cycles required for the fluorescent signal to cross the threshold in RT-PCR. The relative expression levels of each target miRNA were calculated according to $\Delta\Delta^{\text{Ct}}$ method\(^{(18)}\) using Rotor-Gene Q series Software\(^2.1\)(Qiagen, Germany).

Statistical methodology
Analysis of data was done by IBM computer using SPSS (statistical program for social science version 18). Values were expressed as mean ± standard deviation (SD), or median and interquartile range when appropriate. Comparisons of serum miRNA expression levels were performed by applying Mann-Whitney test (between 2 groups) and Kruskal-Wallis test (for 3 or more groups). The data were regarded as significantly different at P value <0.05. To assess the diagnostic accuracy of miR-29a and miR-361-5p, a receiver operating characteristic (ROC) curve analysis was performed. The area under the ROC curve (AUC) and 95% confidence interval (CI) were then estimated to determine the specificity and sensitivity of TB infection prediction.

RESULTS
Demographic and clinical characteristics of different studied groups
The demographic and clinical characteristics of the participants are shown in Table 1. A total of 50 participants were
recruited into this study including 20 TB infected patients (13 men and 7 women; mean age, 36.70 ± 11.49 years), 15 patients diagnosed (clinically, radiologically and laboratory) with pulmonary infection caused by bacteria other than M. Tuberculosis (11 men and 4 women; mean age, 31.13 ± 9.88 years), and 15 healthy controls (13 men and 2 women; mean age, 20.67±4.50 years). There were no significant differences among the groups in terms of age or gender.

Table (1): Demographic and clinical characteristics of different studied groups.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group I (TB infected, n=20)</th>
<th>Group II (other bacterial infection, n=15)</th>
<th>Group III (healthy controls, n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (no. male/female)</td>
<td>13/7</td>
<td>11/4</td>
<td>13/2</td>
</tr>
<tr>
<td>Age, mean (range) yr</td>
<td>36.70 ± 11.49 (18-65)</td>
<td>31.13 ± 9.88 (16-52)</td>
<td>20.67 ± 4.50 (14-30)</td>
</tr>
<tr>
<td>Smear test proven</td>
<td>20</td>
<td>0</td>
<td>N/A</td>
</tr>
<tr>
<td>Sputum culture proven</td>
<td>20</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Primary pulmonary lesion by radiography</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>present</td>
<td>16</td>
<td>12</td>
<td>N/A</td>
</tr>
<tr>
<td>absent</td>
<td>4</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>BCG vaccination</td>
<td>yes</td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td>no</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

TB, tuberculosis; BCG, Bacillus Calmette-Guérin vaccine; NA, not applicable.

Serum expression levels of miR-29a and miR-361-5p studied groups

Table 2 & 3 show comparison of miRNA serum expression levels between TB infected (group I), other bacterial infection (group II) and healthy subjects (group III). When comparing each 2 groups separately, we found the levels of serum miR-29a were significantly higher in TB infected patients compared to healthy subjects (P<0.01) and other bacterial infection group (P=0.03). The comparison between the three groups revealed highly significant difference (P<0.01) with miR-29a expression level increased in TB infected group. On the other hand, serum miR-361-5p levels were significantly higher in TB infected group compared to healthy subjects (P=0.03), but no significant difference than those with other bacterial infection (P=0.49). There was no significant difference of miR-361-5p expression level between the three groups (P=0.05).

Table (2): Comparison of miR-29a serum expression levels among different studied groups.

<table>
<thead>
<tr>
<th>MiRNA</th>
<th>Groups</th>
<th>No.</th>
<th>Mean±SD</th>
<th>Median</th>
<th>Interquartile range</th>
<th>Kruskal-Wallis test (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>miR-29a</td>
<td>Group I</td>
<td>20</td>
<td>8.069794E5±2.1878240E</td>
<td>8429.100</td>
<td>340713.517</td>
<td>&lt;0.01 (HS)</td>
</tr>
<tr>
<td></td>
<td>Group II</td>
<td>15</td>
<td>450.505200±1.3551788E3</td>
<td>0.400</td>
<td>59.580</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Group III</td>
<td>15</td>
<td>0.005733±0.0104092</td>
<td>0.001</td>
<td>0.010</td>
<td></td>
</tr>
</tbody>
</table>

Mann-Whitney Test (P-value)

<table>
<thead>
<tr>
<th>Group I versus Group II</th>
<th>Group I versus Group III</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.01 (HS)</td>
<td>0.03 (S)</td>
</tr>
</tbody>
</table>

HS: Highly statistically significant difference (P-value <0.01).
S: Statistically significant difference (P-value <0.05).
Table (3): Comparison of miR-361-5p serum expression levels among different studied groups.

<table>
<thead>
<tr>
<th>MiRNA</th>
<th>Groups</th>
<th>No.</th>
<th>Mean±SD</th>
<th>Median</th>
<th>Interquartile range</th>
<th>Kruskal-Wallis test (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group I</td>
<td>20</td>
<td>9.599475E+2</td>
<td>691.335</td>
<td>256566.795</td>
<td></td>
</tr>
<tr>
<td>miR-361-5p</td>
<td>Group II</td>
<td>15</td>
<td>1.652877E+5</td>
<td>10.700</td>
<td>2715.000</td>
<td>P=0.05 (NS)</td>
</tr>
<tr>
<td></td>
<td>Group III</td>
<td>15</td>
<td>1.143400E+2</td>
<td>0.010</td>
<td>0.200</td>
<td></td>
</tr>
</tbody>
</table>

Mann-Whitney Test (P-value)

<table>
<thead>
<tr>
<th>Group I versus Group II</th>
<th>Group I versus Group III</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.03 (S)</td>
<td>0.49 (NS)</td>
</tr>
</tbody>
</table>

S: Statistically significant difference (P-value <0.05).
NS: Statistically non-significant difference.

**ROC curve analysis**

The diagnostic performance of miR-29a in discriminating the TB infected group from the healthy subjects and other bacterial infection was evaluated. The analysis demonstrated that, miR-29a exhibited an excellent distinguishing efficiency in discriminating the TB infected group from the healthy subjects (AUC =0.90, 95% CI, 0.77-1.00; sensitivity=85%; specificity =87%, fig 2A), while it exhibited a good distinguishing efficiency in discriminating the TB infected group from other bacterial infection and healthy subjects (AUC =0.81, 95% CI, 0.67-0.95, sensitivity & specificity =70%, fig 2B).

The diagnostic performance of miR-361-5p in discriminating the TB infected group from the healthy subjects and other bacterial infection was also evaluated. The analysis demonstrated that miR-361-5p, exhibited a fair distinguishing efficiency in discriminating the TB infected group from the healthy subjects (AUC =0.72, 95% CI, 0.55-0.89; sensitivity=70%; specificity =60%, fig 3A), while it exhibited a poor distinguishing efficiency in discriminating the TB infected group from other bacterial infection and healthy subjects (AUC =0.64, 95% CI, 0.479-0.807, sensitivity=60% & specificity =57%, fig 3B).

![Figure (2): ROC curves for the ability of serum miR-29a to differentiate pulmonary TB patients from (A)healthy subjects,(B)control groups(other bacterial infection group+ healthy control group).](image-url)
DISCUSSION

Routine clinical methods for diagnosing TB, involving radiography, culture of sputum and the tuberculin skin test, have many shortcomings. Finding new biomarkers in tuberculosis is not only necessary for diagnosing patients with TB, but also for the staging or classification of TB, TB prognosis, and TB drug and vaccine trials.

TB is classified as a granulomatous inflammatory condition. Macrophages, T lymphocytes, B lymphocytes and fibroblasts are among the cells that aggregate to form granulomas, with lymphocytes surrounding the infected macrophages. All of these cells secrete miRNAs into the serum. It was hypothesized that serum miRNAs were derived from the release of infected epithelial cells as well as from other cell types, including immune cells. The target gene prediction results also showed the miRNAs might involve in regulation of anti-TB immunity, respiratory system development and lung development. Therefore, analysis of a cluster of *M. tuberculosis*- associated miRNAs in sera will notably improve the diagnosis of TB infection although the underlying mechanism requires further investigation.

The results of our study showed that TB infected group had significantly elevated expression of serum miR-29-a compared to healthy subjects (P<0.01) and other bacterial infection group (P=0.03). The comparison between the three groups revealed highly significant difference with miR-29a expression level increased in TB infected group. ROC curve analysis was performed to further evaluate the diagnostic value of miR29a as a biomarker for active pulmonary TB. MiR-29a exhibited an excellent distinguishing efficiency in discriminating the TB infected group from the healthy subjects (AUC =0.90; sensitivity= 85%; specificity= 87%). This agreed with Fu et al., who reported increased miR-29a in serum of the active TB group compared with the healthy controls. To validate whether there was consistency between serum and sputum, they also detected the expression of miR-29a in the TB sputum, and found it was present in higher abundance than in that of the healthy controls. They reported that the AUC of miR-29a was 0.831, which reflected that miR-29a has great potential as biomarker to detect active pulmonary TB infection, with sensitivity of 83% and specificity of 80%, respectively. In contrast, Qi et al. didn’t observe miR-29a showing significantly difference in qRT-PCR results, and attributed that to the differences in microarray system, sample size, etc.

Our study differs from the study by Fu et al., that we included not only TB, and healthy group but other bacterial infection group as well. We observed that miR-29a exhibited a good distinguishing efficiency in discriminating the TB infected group from healthy controls as well as other bacterial infection group (AUC =0.81; sensitivity & specificity = 70%). The expression level of studied miRNAs may be elevated in the other bacterial infection group, thus results of this group should be considered, to verify if the analyzed microRNAs are elevated specifically in TB and can discriminate it from other bacterial infection as well as healthy controls.
Along the same line but using different samples, Yi et al.\(^{(10)}\) reported that miR-29a was overexpressed in TB infected sputum compared with controls. Fu et al.\(^{(20)}\), showed that miR-29a was overexpressed in CD4+T cells from active TB group compared with the healthy controls, while miR-29a was down-regulated in the LTBI group compared with the healthy controls. Also, Zhang et al.\(^{(4)}\), found miR-29a was upregulated in serum from patients with active TB compared with the other controls (LTBI, BCG-inoculated and un-inoculated individuals).

Several studies explored the possible role of miR-29a in TB infection. MiR-29a was shown to directly target negative regulators of Wnt signaling, and Wnt was known to trigger macrophage inflammatory responses\(^{(22)}\). A study by Sharbati et al.\(^{(22)}\), showed that miR-29a was specifically upregulated after the mycobacterial infection of human macrophages. MiR-29 suppresses immune responses to \textit{M. tuberculosis} by downregulating IFN-\(\gamma\)\(^{(15)}\). Besides targeting 3'UTR IFN-\(\gamma\) mRNA, miR-29a promotes the association of IFN-\(\gamma\) mRNA with Argonaute 2 (Ago2) protein to form an RNA-induced silencing complex and subsequently suppressed the IFN-\(\gamma\) expression posttranscriptionally. Along the same line, Fu et al.\(^{(20)}\) showed that IFN-\(\gamma\) mRNA levels were down-regulated in both the LTBI group and the active TB group compared with the healthy controls, and IFN-\(\gamma\) mRNA expression was decreased more in the active TB group compared with the LTBI group, which could partly explain one mechanism that overexpressed miR-29 in the active TB group might inhibit CD4+ T cells response to TB infection by suppression of IFN-\(\gamma\)-mediated signaling pathway. MiR-29 mimics (synthetic miRNAs that mimic the function of endogenous miR-29) were used to further assay the effect of increased miR-29 level on IFN-\(\gamma\) production in activated CD4+ T cells with purified protein derivative (PPD) in vitro. They found that miR-29 mimics significantly inhibited IFN-\(\gamma\) production in activated CD4+ T cells with PPD.

Moreover, several reports have indicated that miR-29 also targets the antiapoptotic proteins B-cell lymphoma 2 (Bcl-2) and myeloid cell leukemia-1 (Mcl-1), the kinase p85a and the GTP-binding protein Cdc42, thus suggesting a central role for miR-29 in regulating the apoptotic pathway in immune cells. Therefore, overexpressed miR-29 in TB infection partly explain one mechanism by which \textit{M. tuberculosis} avoids macrophage digestion through inhibition of IFN-\(\gamma\) and increasing apoptosis of cells involved anti-tuberculosis responses\(^{(3)}\). A contrasting phenomenon occurred in a non-virulent \textit{Mycobacterium} species infection model. \textit{Mycobacterium bovis} Bacillus Calmette-Guerin (BCG) down regulated miR-29 expression and induced IFN-\(\gamma\) expression in NK cells and T cells. This result indicates miR-29 inhibition may have facilitated IFN-\(\gamma\) production by these T cells and expression of miR-29 is influenced by Mycobacterium species-specific virulence\(^{(15)}\). All these data suggest that miR-29a might act as a negative regulator of immune response against TB infection and illustrate the potential of using microRNA modulation for the development of approaches for prevention and therapy against infection.

We observed that serum miR-361-5p levels were significantly higher in TB infected group compared to healthy subjects (P=0.03), but no significant difference than those with other bacterial infection (P=0.49). There was no significant difference of miR-361-5p expression level between the three groups (P=0.05). ROC analysis demonstrated that miR-361-5p, exhibited a fair distinguishing efficiency in discriminating the TB infected group from the healthy subjects (AUC =0.72; sensitivity=70%; specificity=60%), while it exhibited a poor distinguishing efficiency in discriminating the TB infected group from healthy subjects as well as other bacterial infection group (AUC =0.64; sensitivity=60%&specificity=57%). Our results partly agreed with Qi et al.\(^{(10)}\), who reported that miR-361-5p was overexpressed in TB infected sera compared to healthy controls, though they also observed that miR-361-5p was also significantly lower in TB infected sera compared to other infection group (\textit{Bordetella pertussis}, varicella-zoster virus, and enterovirus). They showed that the ROC curve of miR-361-5p exhibited a moderate distinguishing efficiency with an AUC value of 0.848. On the other hand, Maertzdorf et al.\(^{(23)}\), showed that miR-361-5p was under-expressed in TB patients. This discrepancy may be due to the analysis of different sample types (peripheral blood mononuclear cells and serum). Fu et al.\(^{(20)}\) reported that miR361-5p was downregulated in CD4+T cells from latent TB group compared with the active TB group.

Qi et al.\(^{(10)}\) further investigated the possible function of miR-361-5p, by studying the target genes. They found some genes targeted by miR-361-5p involved in immune system development, other genes are associated with respiratory system development. For example, among predicted genes (SP1, PGM3, IL10, PIK3R1, RPA1, TGFβ2, TGFR1, WEGFA)
targeted by miR-361-5p, SP-1 transcription factor (SP1) was a key signaling pathway for IL-10 expression in the lung (17). Previous studies demonstrated that miR-361-5p was relatively abundant in bleomycin-induced fibrosis in mouse lungs and that its potential target genes may contribute to the understanding of the molecular mechanisms of lung injury and fibrosis (16).

In conclusion, the present study demonstrated that the expression of miR-29a in serum was highly significantly elevated in TB infected patients. The diagnostic performance of miR-29a is better than miR-361-5p for pulmonary TB. We recommend large scale studies to investigate the molecular role of both miRNAs in TB infection. Also, further studies are needed to assess the diagnostic efficiency of miR-29a as a biomarker for different situations including protection by vaccination, discrimination of latent and active disease, assessment of treatment outcome, and relapse risk.

REFERENCES


الجزء الصغير من الحمض النووي الريبوزي 29a و الجزء الصغير من الحمض النووي الريبوزي 361p

ا. الكشف عن الجزء الصغير من الحمض النووي الريبوزي 29a و الجزء الصغير من الحمض النووي الريبوزي 361p في مصل مرضى الدربون الرئوي. وهذه المحاولة تتضمن نقل نورما كدلالات حيوية محتملة للتشفير. وقد أجريت الدراسة باستخدام تقنية الريبوزوترونق (RT-PCR) للتعرف على الجزء الصغير من الحمض النووي الريبوزي 29a و الجزء الصغير من الحمض النووي الريبوزي 361p في عينات مصل مرضى الدربون الرئوي. تم استخدام مبني روك لتحليل تعابير ودقة التشخيص للجزء الصغير من الحمض النووي الريبوزي 29a و الجزء الصغير من الحمض النووي الريبوزي 361p.

وقد كشف الإنتاج النتائج: وجد أن تعبير الجزء الصغير من الحمض النووي الريبوزي 361p أعلى بصورة ملمحة في مصل مرضى الدربون الرئوي مقابل مريضي النوبة. بينما لا يوجد فرق في تعبير الجزء الصغير من الحمض النووي الريبوزي 29a. أظهرت النتائج أن الجزء الصغير من الحمض النووي الريبوزي 29a و 361p له كفاءة تشخيصية جيدة في الفحص بين مرضى الدربون الرئوي و المريضي النوبة. بينما الجزء الصغير من الحمض النووي الريبوزي 29a و 361p ليس له كفاءة تشخيصية.

أوضح النتائج الإحصائيات زاوية معاينة تعبير الجزء الصغير من الحمض النووي الريبوزي 29a في مصل مرضى الدربون. استخدام مقياس التشخيص للدرر الأفراد من الجزء الصغير للحمض النووي الريبوزي 29a - 361p. ويعتمد على تقييم الفحص الاجتماعي للدربون الرئوي و 361p. 

وتشمل هذه الدراسات الإجراءات المهمة للتنبؤ ب التطبيق الطبي للمضادات الحيوية في حالات التطور، التزويق بين المرض النشط والدربون الكامنة. وتقييم نتائج العلاج.

الدراة

ابراهيم دالاو، سها عبد الرحمن الهادي، نوراء شعبان السها، عادت الدين عبد الرحيم قراعة، ونجوى محمود أحمد، محمد الجدي، محمد محترم، محمد عبد الرؤف، محمد محمد الطيب.

قسم الميكروبايوتولوجيا الطبية والمناعة، قسم الصدر، كلية الطب، جامعة عين شمس، دمشق، سوريا، 30 أكتوبر، 2014.