AJPMHS GLOBAL RESEARCH NETWORK

AMERICAN Journal of Pediatric Medicine and Health Sciences
Volume 01, Issue 10, 2023 ISSN (E): 2993-2149

Diagnosis of Candida Pneumonia in Young Children

Nabieva Zumrat Tukhtaevna, Khodjaeva Nafisa Abaevna
Bukhara State medical institute

Abstract: Fungal infections are common in pediatric intensive care units (PICUs), but the monitoring methods are limited. This study analyzed the differences in clinical features, diagnosis, and treatment between PICU patients with and without fungal infection.

Methods: This retrospective study analyzed PICU patients at the Child Health Hospital of Bukhara diagnosed with severe pneumonia between January 2019 and January 2023. The patients were divided into the fungal (F) and non-fungal (NF) infection groups. Levels of 1,3-beta-D-glucan (BDG) and galactomannan (GM) in serum and bronchoalveolar lavage fluid (BALF) were analyzed. Chest computed tomography (CT) images were reviewed.

Results: A total of 157 patients were included. In the F group, fever, moist rales, coarse rales, shortness of breath, and sepsis were more common (all $P < 0.05$); PICU time, hospitalization duration, and BDG- and GM-positive rates in serum and BALF were all significantly higher than in the NF group (all $P < 0.05$). The BDG- and GM-positive rates in serum and BALF were higher in the F than in the NF group (all $P < 0.05$). The abnormal lymphocyte ratios in serum were higher in the F group (all $P < 0.05$). Wedge-shaped, patchy, streaky shadows and subpleural reticulation were higher in CT images of the F group (all $P < 0.05$). Tracheobronchial stenosis was more common in pulmonary fibroscopy results of the F group ($P = 0.04$).

Conclusion: PICU pneumonia patients with fungal infection have specific clinical and laboratory features compared with those without fungal infection, including higher rates of BALF, serum BDG, GM positivity and tracheobronchial stenosis.

Introduction

Fungal infections are common in pediatric intensive care units (PICUs) and neonatal intensive care units (NICUs). Invasive fungal disease is among the main causes of morbidity and mortality of hospitalized pediatric patients, especially premature infants [1–4]. Yeast and mold are the most common clinical fungal pathogens. According to a report by the Centers for Disease Control and Prevention, fungal infection is the sixth largest cause of nosocomial infections, and Candida spp. is the fourth-most common pathogen responsible for hospital-acquired infections [5]. In the NICU, fungal infection is the third most common cause of mortality, with a rate as high as 20–40% [6]. In 2000, nosocomial fungal infections increased significantly compared with 2001–2004 (24.4 vs. 13.9%) [7]. Candidemia ranked fourth in the United States and seventh in Europe among blood infections responsible for the high mortality rate among children [8].

With improvements in diagnostic technologies and treatment methods, the incidence of fungal infections has shown a downward trend in recent years, but its mortality remains high [1, 4]. Unfortunately, the methods available to monitor fungal infections are limited and definitive diagnosis in many cases is still difficult. Despite their low sensitivity and long delays before

providing results, the fungal culture of blood, body fluids, and respiratory secretions is still considered the gold standard.

Novel methods have shown promise, including serum marker tests such as the G test and galactomannan (GM) test, polymerase chain reaction (PCR), matrix-assisted laser desorption/ionization-time of flight, high-throughput pathogen sequencing, and other molecular approaches [9–12]. Because the diagnostic accuracy of culture and imaging is low for patients with fungal infections [12, 43], they are often misdiagnosed as tumors, tuberculosis, or inflammatory lesions [14–36], resulting in delayed treatment. Bronchoscopic manifestations and testing of the bronchoalveolar lavage fluid (BALF) in children with pulmonary fungal infections could have a high diagnostic accuracy [17, 18].

Accurate identification and timely diagnosis of fungal infections are crucial to the early control of the disease, as well as reducing medical costs and the economic burden on society and families. Therefore, this paper summarizes the clinical diagnosis and treatment of patients in the PICU of the Child Health Hospital from January 1, 2019 to January 1, 2023 and analyzes the general clinical manifestations, chest computed tomography (CT), laboratory examination, fiberoptic bronchoscopy examination, and BALF. The results could provide a reference for medical practitioners.

Patients and Methods

This retrospective study examined the data of 157 patients with proven or probable pulmonary fungal infection admitted to the PICU of the Child Health Hospital, between January 1, 2019, to January 1, 2023. All data were prospectively collected in a database. The study was approved by Child Health Hospital of Bukhara. Informed consent was waived due to the retrospective nature of the study.

According to the European Organization for Research and Treatment of Cancer/Mycoses Study Group, fungal diagnostic criteria include clinically diagnosed and suspected patients [12, 19]. Therefore, the inclusion criteria were (1) patients younger than 18 years and (2) patients who met the diagnostic criteria of severe pneumonia in community-acquired pneumonia [20]. Patients with incomplete data, a hospital stay of < 3 days and serum and BALF were not simultaneously tested for 1,3-beta-D-glucan (BDG), and GM were excluded.

Data Collection and Grouping

Demographic data and clinical characteristics such as clinical manifestation and acute physiology and chronic health evaluation (APACHE) score were obtained from medical records. Routine blood biochemical tests, chest CT, and serum 1,3-beta-D-glucan (BDG) and GM tests were performed on days 1 and 2 of PICU admission. For suspected patients and those with unfavorable outcomes after routine anti-infection treatment, fiberoptic bronchoscopy and alveolar lavage were performed from days 3 to 7; BALF was tested using BDG and GM tests. Chest CT was performed for all patients after 10–14 days of antifungal infection treatment . All test results and clinical data were recorded and retrospectively analyzed. Patients were divided into fungal (F) and non-fungal (NF) groups, depending on the presence or absence of fungal infection. The diagnostic criteria for fungal infection were the child had a history of cough, wheezing, and fever, pulmonary rales and sounds, no obvious improvement with antibiotic treatment, pulmonary CT showed signs of fungal infection, fungi were cultivated in blood or BALF, the G and GM tests were positive in blood or BALF, and the condition was significantly improved with antifungal treatment [21–23].

The GM test was performed to detect GM levels in serum and BALF samples using the one-step enzyme immunoassay sandwich method (Aspergillus antigen detection kit). The BDG test was mainly performed to detect BDG in serum and BALF samples using the dynamic turbidimetric method (fungal dextran detection kit). All tests were conducted following the manufacturer's instructions.

Serum GM > 0.5, BALF GM > 0.7, serum BDG > 100 pg/mL, and BALF BDG > 200 pg/mL were defined as positive values for fungal infection [9, 20].

Chest CT Scan and Interpretation

All patients were placed in the supine position and scanned using a 64-row multi-slice spiral CT. Chest scans were obtained at 1.25-mm intervals using 1.5-mm collimation and were reconstructed with a high-spatial-frequency algorithm. The images were photographed at window settings appropriate for assessing the lung parenchyma (window level, –600 Hounsfield units; window width, 1,600 Hounsfield units). The CT images were retrospectively reviewed by two experienced deputy chief radiologists. The pulmonary nodules or masses, wedge shadow, and consolidation shadow were recorded.

Fiberoptic Bronchoscopy Examination and Interpretation

Fiberoptic bronchoscopy was performed by a deputy director or a senior doctor using an Olympus fiberoptic bronchoscope. All patients who required bronchoscopy provided informed consent obtained from their parents prior to the treatment (excluding those with interfering factors, such as those receiving antibiotics and antifungal treatment). Routine bronchoscopic alveolar lavage was then performed, and their heart rate, oxygen saturation, and blood pressure were monitored. Under general anesthesia with propofol, 2% lidocaine was locally infused into the larynx via the fiberoptic bronchoscope. The top of the fiberoptic bronchoscope was in close contact with the bronchial opening of the lung lobe with abnormal imaging; sterile sodium chloride (0.5–1 mL/kg each time, 15–30 mL in total, at 37°C) was then rapidly injected through the biopsy port. The recovery rate was 40–60%. Furthermore, 50–60 mmHg (1 mmHg = 0.133 kPa) negative pressure suction was applied, and the total amount of lavage fluid was recovered and recorded. The recovered lavage fluid was placed in a uniform sterile container without a heat source and sent for timely inspection.

Pneumonia recovery was defined as the resolution or less cough, wheezing, or fever; lung imaging showed that the infection changes disappeared; the BDG and GM levels became normal. Improved pneumonia was defined as decreased cough and wheezing; lung CT still showed lung shadow (<50%); the GM and BDG levels were partially or completely normal. Uncured was defined as no change or improvement was less than 50%, i.e., lung shadow > 50%.

Statistical Methods

IBM SPSS statistics 24 (IBM, Armonk, NY, United States) was used for analysis. The categorical variables are presented as frequencies and percentages [n (%)] and were compared between groups using the chi-square test or continuous correction method if the effective value was < 5. The continuous variables in accordance with a normal distribution were displayed as mean ± standard deviation (SD) and were analyzed using an independent sample t-test; those not in accordance with a normal distribution are displayed as medians (ranges) and were analyzed using the Mann–Whitney U-test. $P < 0.05$ was considered statistically significant.

Results

General Data and Clinical Features

Of the total 357 patients in the PICU, 169 were in the F group, and 188 were in the NF group. The incidence of fever (56.2 vs. 42.6%, $P = 0.01$), moist rales (46.2 vs. 33.0%, $P < 0.01$), coarse rales (71.6 vs. 55.9%, $P < 0.01$), shortness of breath (79.3 vs. 63.9%, $P < 0.01$), and sepsis (60.9 vs. 44.7%, $P < 0.01$) were higher in the F group than in the NF group, while wheezing rale (50.9 vs. 67.6%, $P < 0.01$) was lower. Furthermore, the days in the hospital and PICU were significantly increased (days in PICU: 12.80 ± 9.20 vs. 9.91 ± 6.84 days, $P < 0.01$; duration of hospital stay: 19.55 ± 9.29 vs. 15.93 ± 9.23 days, $P < 0.01$; Table 1).

Clinical manifestation	F group (*n* = 169)	NF group (*n* = 188)	T	*P*
Male/female	107/62	124/64	0.27	0.60
Age (months)	14.75 ± 21.60	16.46 ± 18.00	1.22	0.22
Weight (kg)	9.24 ± 5.17	10.06 ± 6.48	1.32	0.19
Fever	95 (56.2)	80 (42.6)	6.65	0.01
Fever duration (days)	3.27 ± 7.27	2.45 ± 4.37	1.26	0.21
Cough	153 (90.5)	160 (85.1)	2.43	0.12
Cough duration (days)	9.30 ± 9.83	7.73 ± 8.82	1.58	0.11
Wheezing	54 (32.0)	66 (35.1)	0.40	0.53
Wheezing duration (days)	2.41 ± 5.05	2.70 ± 6.05	0.50	0.62
Distress	56 (33.1)	76 (40.4)	2.03	0.16
Distress duration (days)	0.82 ± 2.43	0.75 ± 1.59	0.36	0.72
Moist rales	78 (46.2)	62 (33.0)	20.17	< 0.01
Coarse rales	121 (71.6)	105 (55.9)	9.50	< 0.01
Wheezing rale	86 (50.9)	127 (67.6)	10.27	< 0.01
Shortness of breath	134 (79.3)	120 (63.9)	10.36	< 0.01
APACHE	98.07 ± 6.46	99.48 ± 6.17	2.11	0.04
Sepsis	103 (60.9)	84 (44.7)	9.44	< 0.01
Septic shock	14 (8.3)	10 (5.3)	1.25	0.26
Mechanical ventilation	44 (26.0)	33 (17.6)	3.79	0.05
Blood purification	6 (3.6)	4 (2.1)	0.24	0.62
Basic diseases				
Premature delivery	22 (13.0)	30 (16.0)	0.62	0.43
Malnutrition	10 (5.9)	5 (2.7)	2.35	0.13
Bronchopulmonary dysplasia	6 (3.6)	3 (1.6)	1.38	0.24
Congenital heart disease	10 (5.9)	9 (4.8)	0.23	0.64
Length of stay (days)	19.6 ± 9.3	15.8 ± 8.2	4.1	< 0.01
Days in PICU (days)	12.8 ± 9.2	9.9 ± 6.8	4.8	< 0.01
Recovery rate	121 (71.6)	125 (66.5)	1.3	0.26
Mortality	2 (1.2)	2 (1.1)	0	> 0.99

Data are expressed as mean ± standard deviation or n (%).
F group, fungal infection group; NF group, non-fungal infection group; APACHE, Acute Physiology and Chronic Health Evaluation scoring system; PICU, pediatric intensive care unit.

TABLE 1. Characteristics of the patients.

Results of the BDG and GM Tests

The BDG and GM values of serum and BALF in the F group were significantly higher than those in the NF group. More patients in the F group had positive serum BDG and GM than in the NF group (BDG: 20.7 vs. 5.9%; GM: 11.8 vs. 4.3%; both P < 0.01). Similarly, more patients in the F group had positive BALF BDG and GM than in the NF group (BDG: 50.9 vs. 18.6%; GM: 39.1 vs. 17.0%; both P < 0.01). Fewer patients in the F group had negative serum BDG and GM than the NF group (67.5 vs. 87.8%, P < 0.01). In addition, fewer patients in the F group had negative serum and BALF BDG and GM than the NF group (20.1 vs. 62.8%, P < 0.01.

Pathogens

Results of the mycoplasma, adenovirus, blood culture, sputum culture, and lavage fluid culture showed no significant specificity in the F group compared with the NF group.

Routine Blood Tests

The routine blood test results were compared between the F and NF groups. The proportion of C3, serum albumin, prealbumin, prothrombin, and blood monocytes was significantly lower in the F group, whereas the proportion of hydroxybutyric acid, lactate dehydrogenase, and abnormal lymphocytes in blood smear was significantly higher in the F group than that in the NF group (all $P < 0.05$).

Chest CT Imaging and Fibroscopy of Both Groups

Chest CT imagining revealed that the F group showed a significant increase in wedge-shaped, patchy, streaky shadow and subpleural reticulation (all $P < 0.05$); however, halo sign, cavity, and consolidation did not significantly increase in the F group.

Pulmonary fibroscopy findings were compared between both groups . Changes in the bronchoscopy results observed in the F group could contain bronchial congestion, edema, paleness, necrosis, and bleeding. The lavage fluid could contain pus and blood and have a sticky, jelly, or foamy consistency. Tracheobronchial stenosis was more common in the F group than in the NF group (55.0 vs. 44.1%, $P = 0.04$). There was no significant difference in the properties of lavage fluid and tracheomalacia between the two groups.

Conclusion

The factors associated with fungal infections should be considered when evaluating pediatric patients. PICU pneumonia patients with fungal infection have specific clinical and laboratory features compared with those without fungal infection, including higher rates of BALF, serum BDG, GM positivity and tracheobronchial stenosis. Using antifungal therapies combined with tests like serum and BALF BDG and GM could enable a timely diagnosis of pulmonary fungal infections, possibly improving prognosis. Future prospective studies should examine the diagnosis and prognosis of PICU pneumonia patients with fungal infection.

References

1. Steinbach WJ, Fisher BT. International collaborative on contemporary epidemiology and diagnosis of invasive fungal disease in children. J Pediatric Infect Dis Soc. (2017) 6:S1–2. doi: 10.1093/jpids/pix039
2. Ahangarkani F, Shokohi T, Rezai MS, Ilkit M, Mahmoodi Nesheli H, Karami H, et al. Epidemiological features of nosocomial candidaemia in neonates, infants and children: a multicentre study in Iran. Mycoses. (2020) 63:382–94.
3. Pfaller MA, Diekema DJ. Epidemiology of invasive candidiasis: a persistent public health problem. Clin Microbiol Rev. (2007) 20:133–63.
4. Pana ZD, Roilides E, Warris A, Groll AH, Zaoutis T. Epidemiology of invasive fungal disease in children. J. Pediatric Infect Dis Soc. (2017) 6:S3–11. doi: 10.1093/jpids/pix046
5. Wisplinghoff H, Ebbers J, Geurtz L, Stefanik D, Major Y, Edmond MB, et al. Nosocomial bloodstream infections due to Candida spp. in the USA: species distribution, clinical features and antifungal susceptibilities. Int J Antimicrob Agents. (2014) 43:78–81. doi: 10.1016/j.ijantimicag.2013.09.005
6. Jantarabenjakul W, Yodkitudomying C, Chindamporn A, Suchartlikitwong P, Anugulruengkitt S, Pancharoen C, et al. Pediatric and neonatal invasive candidiasis: species distribution and mortality rate in a Thai tertiary care hospital. Pediatr Infect Dis J. (2021) 40:96–102.
7. Wen XM, Ren N, Xu XH, Huang X. Distribution and drug resistance of pathogens causing nosocomial infections in national nosocomial infection surveillance network. J Chin Hosp Infect Sci. (2002) 16:241–4.

8. Elmurodova , A. . (2023). ROLE OF CYTOKINES IN THE DEVELOPMENT OF LIVER CIRRHOSIS, WHICH DEVELOPED AS A RESULT OF CHRONIC VIRAL HEPATITIS D. *Евразийский журнал медицинских и естественных наук*, *3*(11), 217–221. извлечено от https://in-academy.uz/index.php/EJMNS/article/view/23842/

9. Elmurodova A.A. (2023). Viral Hepatitis Delta: An Underestimated Threat. *Texas Journal of Medical Science*, *26*, 1–3. Retrieved from https://zienjournals.com/index.php/tjms/article/view/4610

10. Oblokulov Abdurashid Rakhimovich Mukhammadieva Musharraf Ibrokhimovna Sanokulova Sitora Avazovna Khadieva Dora Isakovna. (2023). CLINICAL AND LABORATORY FEATURES OF SPONTANEOUS BACTERIAL PERITONITIS IN PATIENTS WITH VIRAL LIVER CIRRHOSIS. Journal of Advanced Zoology, 44(S2), 3744–3750. Retrieved from http://www.jazindia.com/index.php/jaz/article/view/1716

11. Mukhammadieva M.I. (2022). Modern clinical and biochemical characteristics of liver cirrhosis patients of viral etiology with spontaneous bacterial peritonitis //Texas Journal of Medical Science. – 2022.- P. 86-90

12. Abdulloev Mukhriddin Ziyodulloevich. (2023). Modern Therapy of Viral Hepatitis. Texas Journal of Medical Science, 26, 66–69. Retrieved from https://www.zienjournals.com/index.php/tjms/article/view/4636

13. Abdulloev Mukhriddin Ziyodulloevich. (2023). Modern Therapy of Viral Hepatitis. Texas Journal of Medical Science, 26, 66–69. Retrieved from https://www.zienjournals.com/index.php/tjms/article/view/4636

14. Mukhammadieva M.I. (2023). Вирус этиологияли жигар циррози беморларида спонтан бактериал перитонит билан асоратланишнинг профилактикаси ва давосини такомиллаштириш//Oriental Renaissance: Innovative, educational, natural and social sciences. -2023.-P.947-953.

15. Oblokulov A.R., M.I.Mukhammadieva.(2022). Clinical and biochemical characteristics of liver cirrhosis patients of viral etiology with spontaneous bacterial peritonitis//Academicia Globe: Indersciense Research.-2022.- P. 210-216.

16. M. R., M. ., & S. A., S. . (2022). Features of the Course of Contagious Giardiasis Associated with Giardiasis. Miasto Przyszłości, 26, 186–189. Retrieved from https://miastoprzyszlosci.com.pl/index.php/mp/article/view/464

17. Sanokulova Sitora Avazovna. (2023). COVID-19 IN CHILDREN. Academia Science Repository, 4(06), 25–32. Retrieved from https://academiascience.com/index.php/repo/article/view/843

18. Sanokulova Sitora Avazovna. (2023). Acute Kidney Injury in Critically Ill Cirrhotic Patients with Spontaneous Bacterial Peritonitis. Texas Journal of Medical Science, 25, 65–70. Retrieved from https://zienjournals.com/index.php/tjms/article/view/4502

19. Sanokulova Sitora Avazovna. (2023). Factors of Development of Hepatorenal Syndrome in Patients with Liver Cirrhosis of Viral Etiology. Texas Journal of Medical Science, 26, 4–9. Retrieved from https://www.zienjournals.com/index.php/tjms/article/view/4611

20. Авазовна, С. С. . (2023). Факторы Развития Гепаторенального Синдрома У Больных Циррозом Печени Вирусной Этиологии. AMALIY VA TIBBIYOT FANLARI ILMIY JURNALI, 2(12), 1–8. Retrieved from https://www.sciencebox.uz/index.php/amaltibbiyot/article/view/8673

21. Санокулова, Ситора Авазовна ОСОБЕННОСТИ ТЕЧЕНИЯ КОНТОГИОЗНЫХ ГЕЛЬМИНТОВ АССОЦИИРОВАННОГО С ЛЯМБЛИОЗОМ // ORIENSS. 2023. №2.

URL: https://cyberleninka.ru/article/n/ocobennosti-techeniya-kontogioznyh-gelmintov-assotsiirovannogo-s-lyambliozom (дата обращения: 12.12.2023).

22. Jalilova, A.S. (2022). THE SPREAD OF CIRRHOSIS OF THE LIVER BY ETIOLOGICAL FACTORS. Oriental renaissance: Innovative, educational, natural and social sciences, 2 (6), 253-257.\
23. A. A., E., A. S., D., & A., M. S. (2022). Modern Approaches to Treatment of Chronic Giardiasis. Central Asian Journal of Medical and Natural Science, 3(2), 102-105. Retrieved from https://www.cajmns.centralasianstudies.org/index.php/CAJMNS/article/view/631
24. Облокулов, А., & Муҳаммадиева, М. (2022). КЛИНИКО-ЛАБОРАТОРНАЯ ХАРАКТЕРИСТИКА СПОНТАННОГО БАКТЕРИАЛЬНОГО ПЕРИТОНИТА ПРИ ЦИРРОЗЕ ПЕЧЕНИ ВИРУСНОЙ ЭТИОЛОГИИИ. Журнал вестник врача, 1(3), 66–69. извлечено от https://inlibrary.uz/index.php/doctors_herald/article/view/2016
25. Oblokulova Z.I, Oblokulov A.R, & Jalilova A.S. (2022). Diagnostic Significance of Hepatic Fibrosis in Patients with Extrahepatic Chronic Viral Hepatitis C. Central Asian Journal of Medical and Natural Science, 3(3), 438-443. Retrieved from https://www.cajmns.centralasianstudies.org/index.php/CAJMNS/article/view/806
26. Aslonova.M.R. (2022). Determination of suicidality against the background of Parasitic Diseases in children // INTERNATIONAL JOURNAL OF PHILOSOPHICAL STUDIES AND SOCIAL SCIENCES. – 2022.- P. 9-12.
27. Jalilova, A. S. (2022). Approaches to Etiotropic Therapy of Covid-19 in Outpatient Patients. INTERNATIONAL JOURNAL OF HEALTH SYSTEMS AND MEDICAL SCIENCES, 1(1), 41-44.
28. Mukhtarova Sh.A. (2022) Age-related features of clinical manifestations of giardiasis // International journal of medical sciences and clinical research 2022;17-21.
29. Jalilova A.S. (2022). FEATURES OF CLINICAL MANIFESTATIONS OF CYTOMEGALOVIRUS INFECTION IN CHILDREN. International Journal of Medical Sciences And Clinical Research, 2(09), 12–16. https://doi.org/10.37547/ijmscr/Volume02Issue09-04
30. Raximovich, O. A., Sadilloyevna, J. A., Abdulloyevna, M. S., & Farxodovich , R. F. (2022). Microbiological Indicators of Patients with Confirmed Sars-Cov-2 - Infection. Central Asian Journal of Medical and Natural Science, 3(2), 289-294. https://doi.org/10.17605/OSF.IO/9CFP6
31. Жалилова А. С. Дилноза Саётовна Косимова. Клинико–Лабораторная Характеристика Пациентов С Covid-19 И Предиктор Антибактериальной Терапии //CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES. – 2021. – С. 81-86.
32. Abdulloyevna, M. S. . (2023). Tez-Tez Kasal Bo'lgan Bolalarda O'tkir Respirator Kasalliklarning Klinik-Laboratoriya Xususiyatlari. AMALIY VA TIBBIYOT FANLARI ILMIY JURNALI, 2(12), 29–34. Retrieved from https://sciencebox.uz/index.php/amaltibbiyot/article/view/8680
33. Muxtorova, S. A. (2022). Clinical and laboratoriya features of acute respiratory disease in frequently ill children. Web of scientist: International scientific research journal, 1026-1030.
34. Mukhtarova, S. H. (2022). A.(2022) AGE-RELATED FEATURES OF CLINICAL MANIFESTATIONS OF GIARDIASIS. INTERNATIONAL JOURNAL OF MEDICAL SCIENCES AND CLINICAL RESEARCH, 17-21.
35. Mukhtorova Shokhida Abdulloevna. (2023). Microbiological Indicators of Patients Infected with SarsCov-2. Texas Journal of Medical Science, 21, 41–45. Retrieved from https://www.zienjournals.com/index.php/tjms/article/view/4116

36. Mukhtorova Shokhida Abdulloevna. (2023). CYTOMEGALOVIRUS INFECTIONS IN CHILDREN WITH PRIMARY AND SECONDARY IMMUNE DEFICIENCIES. Academia Science Repository, 4(06), 23–28. Retrieved from http://academiascience.com/index.php/repo/article/view/832

37. Aslonova.M.R. (2023). VITAMIN DEFICIENCY CASES RESULTING FROM PARASITIC DISEASES // Galaxy International Interdisciplinary Research Journal.-2023.- P. 404-409

38. Mukhtorova Shokhida Abdulloevna. (2023). CHARACTERISTIC FEATURES OF THE COURSE OF CITOMEGALOVIRUS INFECTION IN CHILDREN. Galaxy International Interdisciplinary Research Journal, 11(4), 484–487. Retrieved from https://giirj.com/index.php/giirj/article/view/5150..

39. Raximovich, O. A., Sadilloyevna, J. A., Abdulloyevna, M. S., & Farxodovich , R. F. (2022). Microbiological Indicators of Patients with Confirmed Sars-Cov-2 - Infection. *Central Asian Journal of Medical and Natural Science*, *3*(2), 289-294. https://doi.org/10.17605/OSF.IO/9CFP6

40. Ш. А, М. (2023). Профилактика Сезонного Распространения Орви Среди Детей Раннего Возраста. AMALIY VA TIBBIYOT FANLARI ILMIY JURNALI, 2(12), 22–28. Retrieved from https://www.sciencebox.uz/index.php/amaltibbiyot/article/view/8678

41. Карроматов И.Дж., and Аслонова М.Р.. "Салат, латук перспективное лекарственное растение" Биология и интегративная медицина, no. 4, 2018, pp. 120-129.

42. Raximovich, O. A., & Ramazonovna, A. M. (2022). TO IDENTIFY THE CALCIOLOGICAL DEFICIENCY THAT OCCURS AGAINST THE BACKGROUND OF HELMINTHIASIS IN CHILDREN. Central Asian Journal of Medical and Natural Science, 3(2), 91-95. Retrieved from https://www.cajmns.centralasianstudies.org/index.php/CAJMNS/article/view/629

43. M. R., A. . (2022). DETERMINATION OF SUICIDALITY AGAINST THE BACKGROUND OF PARASITIC DISEASES IN CHILDREN. International Journal of Philosophical Studies and Social Sciences, 2(2), 9–12. Retrieved from http://ijpsss.iscience.uz/index.php/ijpsss/article/view/166

44. Рахматова Дилбар Бахридиновна, Аслонова Маржона Рамазоновна Современные методы медицинской реабилитации пациентов с артериальной гипертензией // Биология и интегративная медицина. 2018. №3. URL: https://cyberleninka.ru/article/n/sovremennye-metody-meditsinskoy-reabilitatsii-patsientov-s-arterialnoy-gipertenziey (дата обращения: 16.12.2023).

45. Tukhtaevna N. Z. The Relationship of Tuberculosis and Pneumonia in Children, Clinical Characteristics //INTERNATIONAL JOURNAL OF HEALTH SYSTEMS AND MEDICAL SCIENCES. – 2023. – Т. 2. – №. 5. – С. 168-172.

46. Nabiyeva, Z. . (2023). CLINICAL MANIFESTATIONS OF CHRONIC DISEASES ОРГАНОВ OF THE DIGESTIVE SYSTEM IN CHILDREN. Инновационные исследования в современном мире: теория и практика, 2(15), 27–28. извлечено от https://in-academy.uz/index.php/zdit/article/view/13239

47. Карроматов Иномжон Джураевич, Набиева Зумрад Тухтаевна Адаптоген - элеутерококк, свободоягодник колючий (обзор литературы) // Биология и интегративная медицина. 2017. №11. URL: https://cyberleninka.ru/article/n/adaptogen-eleuterokokk-svobodoyagodnik-kolyuchiy-obzor-literatury (дата обращения: 19.12.2023).

48. Achilova D. N., Amonov R. A., Sharipova L. Kh., Yomgurova O. R., Rustamov B. B. (2021). Clinical, Immunological and Medico-Social Aspects of Allergic Diseases in

Children. Annals of the Romanian Society for Cell Biology, 6736–6740. Retrieved from http://www.annalsofrscb.ro/index.php/journal/article/view/2188

49. Yomgurova Ozoda Rajabturdievna. (2023). Manifestations of Various Diseases and Changes in The Body in Children Suffering from Drug Allergy. Texas Journal of Medical Science, 20, 23–28. Retrieved from https://www.zienjournals.com/index.php/tjms/article/view/3877
50. Yomgurova Ozoda Rajabturdievna. (2023). ALLERGIC REACTIONS AND MEDICINAL PRODUCTS: CONTEMPORARY PRESENTATIONS. Galaxy International Interdisciplinary Research Journal, 11(4), 818–823. Retrieved from https://www.giirj.com/index.php/giirj/article/view/5080