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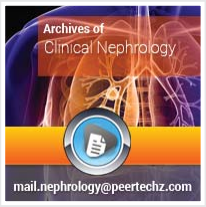

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Review Article

Pneumocystis Jirovecii pneumonia Infection in Immune Compromised Patients, Revisited

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Abstract

A fungal infection, *Pneumocystis jirovecii* pneumonia (PJP) primarily affects immunocompromised individuals, particularly post-transplant patients, leading to high morbidity and mortality rates. This review covers the pathology, risk factors, clinical presentation, diagnostic methods, prophylaxis, and treatment of PJP, with a focus on its implications in kidney transplantation. Local transplantation practices report a low incidence of PJP due to effective prophylaxis and donor-matching strategies. The importance of vigilant monitoring and tailored prophylactic measures is emphasized in preventing PJP.

Introduction

Pneumocystis jirovecii pneumonia (PJP) is a fungus that is a ubiquitous inhabitant, infesting the respiratory system of most human beings. It is one of the major infective micro-organism post-transplantations that harbors exceedingly higher morbidity and mortality. Herein, we are discussing variable aspects of PJP infection post-transplantation, highlighting the local and systemic complications related to PJP infection, PJP prophylaxis, treatment, and our local experience [1].

Pathology

It is a yeast-like fungus, principally an alveolar pathogen. Mainly infecting lungs, and rarely other organs. It forms intra-alveolar eosinophilic foamy masses consisting of multiple cysts containing the fungus. The main reservoir is human beings, shedding from grass and trees might be other sources of the fungus. Most children are infected by the age of 4 years, mostly asymptomatic infection. Colonization is commonly encountered in most of the adults. It might remain dormant in the alveoli and reactivated when the immune system is suppressed, commonly by AIDS or immunosuppressant medications post-transplantation. Reactivation is the main source of infection. However, reinfection is reported as well. Trophozoites spread by inhalation, inhabiting alveoli, attached to type 1 alveolar pneumocytes, to transform subsequently to cystic form. Damage to the lungs is inflicted by the cystic transformation of the fungus and inflammation incited by cell-mediated immunity [1,2].

Fungal stages

It is a non-cultivable extra-cellular fungal infection, formerly considered a protozoa, with multiple phases of the life cycle, all confined to alveolar spaces. Trophozoites is a vegetative stage, thin-walled, amoeboid in shape, single-celled fungus. Cysts of 4-7 mm are thicker walled and exist in a globular pattern, each cyst forms up to 8 sporozoites that are released and aerosolized after rupturing of that sac-like cysts.

Phasic morphologic stages are noticed [3]:

1. **Trophozoite, trophic form:** Presents in clusters, which represents the vegetative state found in alveoli attached to alveolar epithelium. It's the infective form of the fungus.

2. **Sporozoites:** Precystic form.

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3. The cyst transformed from a trophic phase, globular in shape, thick-walled, containing 8 gram-negative sporozoites which are released via rupture of the cysts.

Risk factors

When the immune system is suppressed, PJP is reactivating or re-infecting the patient by invading the alveolar epithelium type one cells, inciting an inflammatory response and transforming to the larger cystic form. The pathogenesis of PJP is dependent on inflammatory response which is robust in non-HIV patients causing prominent symptoms of dyspnea and desaturation with diffuse infiltrative lesions in both lungs. It is predominantly a pulmonary disease, however, extra-pulmonary infection was reported in certain patients who were on aerosolized prophylactic pentamidine, hence hepatosplenomegaly, thyroid, dermal, ophthalmic, and other places where the site of PJP infection. In an immune-competent patient who has an encounter with PJP fungus, a limited inflammatory response is activated which leads to the clearance of the infection [4]. HIV infection, presented as AIDS-defining syndrome, is due to impairment of cell-mediated immunity. It is commonly identified when the CD4 count falls below 200 cells/ml. The risk of attracting PJP infection amounts to 20% - 100% when CD4 counts below 200 cells/ml. Risk has reduced substantially with the institution of prophylaxis antibiotics and ART. HIV-infected patients with other opportunistic infections such as oral thrush, are increasingly vulnerable to PJP even with CD4 above 200 cells/ml. Non-AIDS risk factors include mainly corticosteroid use in rheumatic diseases, connective tissue disease, and vasculitis, post-transplant status, primary immune deficiencies, such as hypogammaglobulinemia, malignancies, particularly hematologic malignancy, and severe malnutrition.

Clinical presentation

Kidney transplantation is the most favored treatment for chronic kidney disease with incomparable long-term survival compared to other modalities. However, the post-transplant immunosuppressed status complicating kidney transplantation portends a soaring risk for opportunistic infections secondary to impaired cell-mediated immunity inflicted by immune suppression protocol and the naturally existent commensal microorganisms that potentially convert to pathogens. Those common inhabitants, dormant micro-organisms flourish to invade and incite an infection that is commonly severe and life-threatening. Common presentations are dyspnea, cough, and sputum. Depending on the underlying disease, variable clinical presentations were recognized, therefore in patients with HIV, symptoms are usually subtle with gradually worsening cough and dyspnea, on the contrary, in other immune-suppressed conditions such as post transplantation, its commonly short-term onset with abrupt symptoms of dyspnea cough and fever, reflecting the level of inflammatory response [5]:

1. Immune-compromised patients
2. Indolent course is prevailing in HIV patients, but commonly abrupt with overwhelming symptoms in non-HIV patients.
3. Sudden presentation of fever in 80%, shivering, dyspnea on exertion in 95%, dry cough in 95% of cases; weight loss, and rarely hemoptysis.
4. Clinically, the examination might be entirely normal in 50% of infected symptomatic patients.
5. Exertional desaturation is a sensitive sign suggestive of underlying PJP.
6. Bilateral crackles with scattered rhonchi are commonly noticed.
7. Extra-pulmonary manifestations are increasingly common in patients on Pentamidine aerosolized prophylaxis and in patients with progressive HIV infection not on prophylaxis.

Extra-pulmonary manifestation

The whole lifecycle is embedded in the alveoli where the fungus is attached to the pneumocyte Type 1 without triggering any inflammatory response. The only identified reservoir is human beings, and transmission is via an airborne route with high tropism to lung tissues. The fungus might continue dormant in the lungs consistently asymptomatic for an extended period when the immune system and cell-mediated immunity are intact in an immunocompetent carrier. The fungus flourishes and invades the pulmonary tissues in the circumstances of immunosuppression such as in HIV-infected patients where it is part of AIDS syndrome or post-organ transplantation status. Commonly encountered in HIV patients when CD4 lymphocytes are less than 200 c/ml. This is consistent with a direct link between cell-mediated immunity suppression and the risk of invasive disease [5,6].

1. Extra-pulmonary PJP is reported in less than 3% of patients.
2. Lymphadenopathy is not a common feature of PJP infection. However, it might be detected in the context of the underlying disease, such as HIV.
3. Thyroid gland: rarely reported to be infected with PJP.
4. Liver involvement, featuring scattered areas of hepatocellular necrosis, sinusoidal and pre-sinusoidal involvement is predominating in some patients to confer obstructive jaundice.
5. Central nervous system CNS: in profoundly immunosuppressed patients, PJP might infect CNS, and clinically present with headaches, convulsions, or non-specific neurological manifestations. Radiological features consistent with PJP infection include brain edema and white matter alteration.
6. Bone marrow involvement results in pancytopenia.

Investigations

Chest X-ray might be entirely normal in symptomatic patients with PJP infection. Commonly, it revealed faint

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reticulo-nodular shadowing bilaterally, 10% - 15% of patients featured normal chest x-ray, 30% inconclusive findings.

In chest X-ray, the characteristics features predominantly suggestive of PJP are: pneumatoceles, multiple, small sized; sub-pleural blebs, diffuse faint interstitial reticular formation, and bilateral peri-hilar involvement. Pleural effusion is very rarely encountered in less than 5% of the patients [6].

High-resolution CT scan

CT scan is more sensitive and specific in detecting PJP pneumonia with cardinal signs of ground glass appearance. Different other findings might be reported in PJP pneumonia. The most sensitive mode of radiology is High-Resolution Computerized Tomography (HRCT) which verifies normal X-ray patients with suspected PJP infection. The classical features of PJP on HRCT are

- The ground glass appearance is the basic finding in PJP. The lesions are perihilar, involving variable pulmonary zones correlated with aerosolized pentamidine prophylaxis administration. Hence, in aerosolized prophylaxis administration patients, the upper poorly ventilated zones are more vulnerable to PJP.
- In non-receivers of aerosolized pentamidine, mid and lower zones are prominently involved.
- Irradiated pulmonary areas are non-infected usually.
- There is peripheral sparing in 40% of cases.
- Reticular formation and septal opacities are frequently encountered, resulting in the so-called crazy pavement radiological appearance, which represents the combined appearance of ground glass and septal thickening, particularly in PJP infection.
- Pneumatocele: reported in 30% of cases, with varied size and thickness. Of its walls.
- Rarely recognized features such as pleural effusion and lymphadenopathy are reported to occur in 10% [7].

Atypical CT findings

Different other findings might be reported in PJP pneumonia. Gallium-67 lung scan is extremely sensitive in detecting PJP infection.

Atypical CT findings are commonly encountered in pentamidine aerosolized patients for prophylaxis, such as consolidation, particularly in non-HIV patients that tend to develop rapidly. Reflective of progressive immune reaction. The nodules that might be complicated by cavitation are notable with co-infection with CMV or Adenovirus. A cystic form with a bilateral presentation that could result in pneumothorax. A negative result is refuting the diagnosis of PJP on a solid base. In PJP, gallium scan features spread bilateral homogenous or heterogenous pulmonary isotope consumption. However, it is nonspecific [7,8].

Differential diagnosis

CMV pneumonia

COVID - 19 pneumonia

Tuberculosis.

Bronchopulmonary Aspergillosis.

Bronchiectasis

Hypersensitivity pneumonitis [9].

Diagnosis

Diagnosis of PJP pneumonia revolved around isolating the fungus in pulmonary secretion or pulmonary tissues. Detection of the fungus or its antigens in induced sputum and broncho-alveolar lavage BAL samples is the cornerstone for diagnosing PJP pneumonia.

As PJP is unculturable and cannot be grown in a culture media, diagnosis is entirely dependent on identifying the micro-organisms in a respiratory specimen such as induced sputum or biomicroscopically collected secretion via BAL [9,10].

Microscopical methods of detection:

1. Light microscopy, applying special stains, trophic form and cystic form can be variably recognized with different stains such as gram-stain, Giemsa, and Papanicolaou for trophozoites and methenamine silver among others, for cyst recovery.
2. The most sensitive microscopical method is immunofluorescent stain labeled antibody against PJP antigen to illuminate trophozoites and cysts similarly [10].

Limitations of microscopical-based diagnosis

Depending on the intensity of micro-organisms in the induced sputum or BAL sample, the sensitivity of the microscopical exam is variable between 50% - 90%. It is usually more sensitive in HIV patients with PJP, owing to massive impairment of cell-mediated immunity, resulting in surplus presence of PJP in sputum or BAL. On the other hand, in non-HIV patients with PJP, the presence of micro-organisms is sparse in any sputum specimen or even BAL sample, making it extremely unlikely to detect microscopically. BAL was reported to be positive in less than 50% of non-HIV patients with PJP [10].

Polymerase chain reaction

When no identifiable organism is reported in BAL secretion with microscopy and histopathological and immunofluorescent staining, diagnosis depends on detecting nucleic acid fragments in the same samples with the amplification technique of Polymerase Chain Reaction (PCR). Single-copy real-time PCR may perfectly differentiate between infection and colonization.

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Polymerase chain reaction can increase the detection of Pneumocystis pneumonia (PCP) in those patients with less micro-organism intensity in induced sputum or BAL samples. It would detect both colonization and genuine pulmonary infection. However, single-copy real-time PCR would detect swiftly PJP infection rather than colonization. On the contrary, nested PCR protocol lacks the capacity to differentiate between PJP infection and colonization in patients with pulmonary PJP.

PCR is generally indicated in patients with clinical features consistent with PJP infection in the setting of immunosuppression, like kidney transplant patients, nevertheless, the microscopy exam with staining is negative for sputum and BAL. Detection of PJP in the specimen is variable in relation to the severity of immunosuppression. Hence, in patients with preserved immune systems, PJP would not be detected microscopically, however, in those patients with diminished immune systems, microscopical examination is more feasible. Therefore, PCR is applicable in patients with non-HIV patients with PCP infection. PCR is commonly increasing the diagnosis of PJP in patients with BAL negative test [11].

Beta D-glucan assay

Beta D-glucan is a fungal cell wall constituent, detected in varied species of fungi. Its detection in patients' serum is supportive of the initial diagnosis of fungal infection. *Aspergillus* and *Candida albicans* are the principal pathogens carriers of Beta D-glucan protein. PJP is positive for the same antigen and could be utilized to verify underlying invasive PJP infection. Its negative predictive value is significant, refuting PJP infection on a solid base. It is more credible in HIV patients with PJP. Its specificity is increasing with a cut-off value of more than 200 pg/ml. When combined with PCR its diagnostic value increases significantly [12].

Histopathology diagnosis

Histological assessment is warranted in patients with inconclusive evidence to support the diagnosis of PJP infection. Particularly indicated in patients suspected of PJP, however, their BAL testing is persistently negative. Commonly, PJP features alveoli with eosinophilic inflammatory exudate. Often, granulomatous lesions with necrotizing or non-necrotizing granulomas might be detected with PJP trophozoites within granulomas [13].

Speculative diagnosis

When a diagnosis of PJP cannot be ascertained owing to a lesser load of PJP fungi in the underlying infective pulmonary tissues and the related specimens thereof. In certain situations, a definite diagnosis of PJP is entirely speculative, because of the difficulty in detecting PJP micro-organisms or even an antigen in induced sputum or BAL secretion. However, clinical scenarios and radiological features are highly suggestive of PJP infection. In addition to the presence of overly sensitive negative results for Beta d-glucan assay which refute the underlying presence of PJP infection. In these situations, an empirical treatment for PJP is advisable given the higher mortality associated with late commencement of therapy. This scenario is commonly encountered in non-HIV-infected patients, in whom immune deficiency is non-massive [12,13].

1. Characteristics of speculative diagnosis:Highly suggestive clinical course.
2. Radiological features of bilateral pulmonary infiltration.
3. Beta d-glucan assay results might determine the nature of the underlying lesion.

PJP prophylaxis

Owing to the higher morbidity and mortality associated with PJP pneumonia, prophylactic antibiotic administration is advocated to prevent reactivation or reinfection in immunocompromised patients. Sulphamethoxazole is the first drug of choice for prophylaxis. Protocols with different doses and duration are advised.

PJP prophylaxis is indicated for all patients with cell-mediated immune deficiency, in particular HIV patients with CD4 lymphocytes below 200/ml, Corticosteroid therapy of more than 20 mg for a month, and patients on cytotoxic therapy. Furthermore, bone marrow transplantation patients and any lymphopenia condition, such as after the use of monoclonal antibodies anti-CD52 Alemtuzumab and anti-CD20 Rituximab induction. Alkylating therapy protocol, such as Cyclophosphamide is another indication [13,14]. Duration of prophylaxis must be extended from 6 to 12 months, or until CD4 improves to more than 200 /ml in particular situations.

Kidney transplant & PJP prophylaxis

It is indicated for a minimum of 4 months post-transplantation by European kidney transplant guidelines. In other protocols, it is advised for 6 to 12 months post-transplantation. Similarly, prophylaxis is indicated after treating acute rejections with high doses of corticosteroids.

Other specific indications for PJP prophylaxis

1. **Desensitization protocol:** It is a risk factor for PJP infection as it involves administering rituximab. Rituximab is a monoclonal antibody against CD20 receptors on B-lymphocytes. Depleting B-lymphocytes impairs immunoglobulins production and thus humoral immunity on one hand, and falter cell-mediated immunity on the other hand as CD4 T lymphocytes depend on B-lymphocytes for activation, as B-lymphocytes present the antigens via its major histocompatibility antigen II MHC.
2. **Co-infection with CMV**: CMV infection is a predisposing factor for co-infection with PJP, as CMV infection induces lymphopenia and further inhibition of cell-mediated immunity due to its targeting of T-lymphocytes and natural killer cells. However, the exact underlying mechanism is not well-identified.

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3. **Low GFR:** Post-transplantation is a risk factor for PJP, attributed to increased blood levels of immune suppressants secondary to decreased clearance.

4. **Older age:** [14].

Trimethoprim-sulfamethoxazol TMP-SMX

It is a first choice for prophylaxis against PJP. It might be implemented in double or single dosing daily or every other day. Whenever allergy is encountered, desensitization strategies must be conducted. In addition to its effect on PJP, It is an effective prophylactic medicine against *Toxoplasma gondii*, pneumococcal, *Nocardia,* and *Listeria* pathogens. Its prophylactic effect was determined to be equivalent to the daily dosing regimen and three times weekly protocol. Bone marrow suppression and nephrotoxicity are major drawbacks of TMR-SMZ.

Features of PJP prophylaxis

In comparison to a drastic reduction of PJP incidence, infection, severity of infection, and mortality rate linked to PJP infection, outweighing the rate of side effects, it's indicative to institute the prophylactic strategy for all of the patients. However, a close observation to detect potential adverse effects is discernible.

Side effects were reported in 3.1% of non-HIV patients. However, an exceedingly higher rate of side effects was encountered in the context of HIV patients with PJP infection. Which might be attributed to massive derangement of the immune system in HIV patients. The incidence of PJP infection was consequently reduced by 85%. Mortality associated with PJP infection was similarly reduced. Leukopenia, Thrombocytopenia, and skin reactions are the most reported adverse reactions.

Owing to its documented effectiveness, desensitization is recommended for those patients allergic to TMP-SMZ, however, it is contraindicated and desensitization is declined in HIV patients who developed Steven Johnson syndrome and toxic epidermal necrolysis [15].

Use of TMP-SMX in special groups of patients

Certain conditions might warrant considerations concerning the implementation of prophylactic TMP-SMX, such as SLE and bone marrow suppression. Hence each patient must be considered as per his merits. There is (no one-size-fits-all).

In patients on special protocols including methotrexate, the use of TMP-SMZ must be precautious, as the risk of bone marrow suppression is mounting. Close follow-up is indicated to uncover the adverse effects.

Long-term use of TMP-SMX was reported to predispose to Systemic Lupus Erythematosus [SLE] relapse. Hence, there is a consensus by rheumatologists of alternatively using Atovaquone instead, for patients with SLE [14,15].

TMP-SMX alternative therapies

Different medications for prophylaxis are advocated with different effectiveness and side effects profiles. However, TMP-SMX is the first drug of choice for prophylaxis and treatment. In patients allergic to TMP-SMX, or in whom adverse effects were reported, alternatives were prescribed, yet with less efficacy. Atovaquone, dapsone with or without pyrimethamine, and aerosolized pentamidine could be prescribed. The patients who are vulnerable to leukopenia, agranulocytosis, thrombocytopenia, and hemolytic anemia, Atovaquone is favored. Similarly, G6PD deficiency must be ruled out before prescribing Dapsone. Dapsone is a preferable alternative due to its less cost-effective profile [16].

TMP-SMX alternatives

Aerosolized pentamidine is not a perfect alternative to TMP-SMX with several drawbacks stemming from its localized effect on the pulmonary system, provoking infections in other areas and systemic infection as well. It's commonly implemented in pediatrics.

The caveats of aerosolized Pentamidine usage are:

1. Its prophylactic effect is localized solely to the pulmonary system.

2. Depending on pulmonary ventilation, the hypo-ventilated apical areas are still increasingly vulnerable to PJP infection.

3. The incidence of extra-pulmonary PJP infection was reportedly increasing with the use of aerosolized pentamidine.

4. Pulmonary tuberculosis transmission was shown to increase in incidence.

Treatment of PCP infection

TMP-SMX is the first choice regardless of the severity of infection. The dose is 15-20 mg/kg (in patients with normal creatinine clearance). Intravenous therapy is advocated for severe diseases.

Criteria for recovery of severe PJP pulmonary disease include:

1. PaO2 of more than 60 mm Hg.

2. Respiratory rate of less than 25/min.

Oral therapy can be re-instituted when both are achieved, and the gastro-intestinal tract is normal. The duration of therapy is principally 21 days. Alternatives for TMP-SMX depend on the severity of the disease. Atovaquone is indicated for mild cases. The oral route is preferred for atovaquone administration. Intravenous Clindamycin and oral Primaquine are indicated for moderate to severe cases. Intravenous TMP-SMX and Dapsone are other options indicated for moderately severe cases.

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Intravenous Pentamidine is as effective as TMP-SMX, however, it is less commonly used in severe cases, as its use is associated with significant toxic adverse effects, pancreatitis, and nephrotoxicity.

Intravenous Clindamycin and oral primaquine are commonly reserved as second-line therapy for severe resistant PCP cases who failed to recover with intra-venous TMP-SMX and Dapsone or intravenous Pentamidine.

Adjuvant therapy with corticosteroids might be indicated in certain cases of HIV with PJP infection [15-17].

Prognosis of PJP infection

The outcome of treatment is variable, the most important determinant of likely prognosis is HIV status. The prognosis and success of treatment depend largely on the etiology of immune suppression, HIV-related *vs.* non-HIV-related, as it is principally governed by the reaction of the immune system toward invading PJP fungi.

The mortality rate of non-HIV infected without antibiotic therapy is 90-100%. Nevertheless, in treated patients, it reached up to 35% - 50%. In contrast, the mortality of treated HIV patients with PJP is dwindling down to a mere 10% - 20%. This apparent contrast might reflect the severity of cell-mediated immunity impairment and blunt response *vs.* profound overwhelming inflammatory reaction in different non-HIV conditions [16,17].

Adverse prognostic features in non –HIV severe PJP infection

Higher mortality and morbidity rates were reported in patients with severe PJP in the context of non-HIV disease, such as hospitalization and ICU admission.

Adverse prognostic features include [18,19]:

1. Soaring APACHE III score on the first day of intensive care unit admission.
2. Respiratory failure.
3. Untimely intubation
4. Time spent on mechanical ventilation.
5. Pneumothorax.
6. Elevation of neutrophil/lymphocytes ratio.

Contentious issues in prophylaxis and treatment

1. Duration on prophylaxis: how long to continue prophylaxis? A question that is answered with conflicts. As the duration is arbitrarily set with no clear indications to continue the same.
2. Best protocol for prophylaxis in HIV and non-HIV patients given the potential toxicity of long-term administration of first-line medicine and the more toxic alternatives.

It is not clearly determined how long prophylaxis must be continued. Owing to the observation of incident cases of PJP, months after withholding of antibody prophylaxis. On the contrary, consistent prolonged use of antibiotics portends an increasing risk of side effects and the emergence of antibiotic resistance strains. On the other hand, prophylaxis duration is more feasible in HIV patients, as CD4 lymphocyte count of more than 200/ml was considered as the cut-off parameter to withhold prophylaxis. This parameter was not firmly concluded in non-HIV immune-compromised patients [18,19].

In general, prophylaxis must continue as long as the patients are immune-suppressed. For those patients who received corticosteroid, or Alkylating agents as part of their immune suppressant protocol, PJP prophylaxis must be continued throughout for an extended period as the immune suppression effect persists for a long time after the induction of immune suppression, and cases of PJP infection were reported months after withdrawal of prophylactic therapy. However, there is no discernible parameter that we consider planning for prophylaxis protocol duration. An exception to this rule is the induction of lympho-depletion instituted with the monoclonal antibodies, Rituximab. In these circumstances, recovery of lymphocytes might be censored by screening CD19-positive cells.

The usual prophylaxis duration is 3-6 months of double-strength TMP-SMX as the first drug of choice. Furthermore, after any acute rejection episode, a full course is reinstituted to cover the profound immune suppression resultant from anti-rejection therapy induction.

Conclusion

In our local transplantation practice, PJP infection was rarely reported. This observation might be attributed to certain factors common to the transplantation program. These factors include life donor transplantation, mostly related donor transplantation, a higher percentage of HLA matching, and the universal application of PJP prophylaxis to all recipients with a double-strength dose for a duration of six months. Due to these factors, the incidence of rejection is significantly low, obviating the need for more aggressive anti-rejection treatment and prophylaxis. Another factor that might influence the map of PJP incidence and occurrence of disease is its prevalence in the community, which could vary from the prevalence of PJP in other countries.

References

1. Fishman JA, Gans H, AST Infectious Diseases Community of Practice. Pneumocystis jiroveci in solid organ transplantation: Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant. 2019;33(9):e13587. Available from: https://doi.org/10.1111/ctr.13587
2. Varnas D, Jankauskienė A. Pneumocystis Jirovecii Pneumonia in a Kidney Transplant Recipient 13 Months after Transplantation: A Case Report and Literature Review. Acta Med Litu. 2021;28(1):136-44. Available from: https://doi.org/10.15388/amed.2020.28.1.5
3. Lee HJ, Kwon HW, Baek JK, Park CH, Seo HK, Hong SK. Risk factors for Pneumocystis pneumonia with acute respiratory failure among kidney

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transplant recipients. BMC Nephrol. 2023 Feb 9;24(1):31. Available from: https://doi.org/10.1186/s12882-023-03071-y

4. Min EK, Lee J, Jeong SJ, Kim DG, Yim SH, Choi MC, et al. Risk factors for late-onset Pneumocystis jirovecii pneumonia in liver transplant recipients. Int J Infect Dis. 2023 Jun;131:166-72. Available from: https://doi.org/10.1016/j.ijid.2023.04.387

5. Liu Z, Zhu J, Li X, Xu W, Li H, Jia Y, et al. Risk factors and treatment experience of Pneumocystic carinii pneumonia after liver transplantation. Chin J Organ Transplant. 2021;12:214-8. Available from: https://pesquisa.bvsalud.org/portal/resource/pt/wpr-911642

6. Meyer AMJ, Sidler D, Hirzel C, Furrer H, Ebner L, Peters AA, et al. Distinct Clinical and Laboratory Patterns of Pneumocystis jirovecii Pneumonia in Renal Transplant Recipients. J Fungi. 2021;7:1072. Available from: https://doi.org/10.3390/jof7121072

7. Bateman M, Oladele R, Kolls JK. Diagnosing Pneumocystis jirovecii pneumonia: A review of current methods and novel approaches. Med Mycol. 2020;58(8):1015-28. Available from: https://doi.org/10.1093/mmy/myaa024

8. Block BL, Mehta T, Ortiz GM, Ferris SP, Vu TH, Huang L, et al. Unusual Radiographic Presentation of Pneumocystis Pneumonia in a Patient with AIDS. Case Rep Infect Dis. 2017;2017:3183525. Available from: https://doi.org/10.1155/2017/3183525

9. Truong J, Ashurst JV. STATpearl. Pneumocystis jirovecii Pneumonia. 2023. Available from: https://pubmed.ncbi.nlm.nih.gov/29493992/

10. Hänsel L, Schumacher J, Denis B, Hamane S, Cornely OA, Koehler P, et al. How to diagnose and treat a patient without human immunodeficiency virus infection having Pneumocystis jirovecii pneumonia. Clin Microbiol Infect. 2023;8:1015-23. Available from: https://doi.org/10.1016/j.cmi.2023.04.015

11. Yang SL, Wen YH, Wu YS, Wang MC, Chang PY, Yang S, et al. Diagnosis of Pneumocystis pneumonia by real-time PCR in patients with various underlying diseases. J Microbiol Immunol Infect. 2020;53(5):785-790. Available from: https://doi.org/10.1016/j.jmii.2019.08.012

12. Overman WF, Ribes JA. (1–3)-β-D-Glucan Assay: A Review of its Laboratory and Clinical Application. Lab Med. 2011;42(11):679–685. Available from: https://doi.org/10.1309/LM8BW8QNV7NZBROG

13. Kim HS, Do SI, Kim YW. Histopathology of Pneumocystis carinii pneumonia in immunocompetent laboratory rats. Exp Ther Med. 2014;8(2):442–446. Available from: https://doi.org/10.3892/etm.2014.1732

14. Caplan AS, Mecoli CA, Micheletti RG. Prophylaxis Against Pneumocystis Pneumonia. JAMA. 2023;330(19):1908-1909. Available from: https://doi.org/10.1001/jama.2023.18862

15. Zhou S, Aitken SL. Prophylaxis Against Pneumocystis Jirovecii Pneumonia in Adults. JAMA. 2023;330(2):182-183. Available from: https://doi.org/10.1001/jama.2023.9844

16. Fragoulis GE, Nikiphorou E, Dey M, Zhao SS, Courvoisier DS, Arnaud L, et al. 2022 EULAR recommendations for screening and prophylaxis of chronic and opportunistic infections in adults with autoimmune inflammatory rheumatic diseases. Ann Rheum Dis. 2022;82:742-753. Available from: https://doi.org/10.1136/ard-2022-223335

17. Ibrahim A, Chattaraj A, Iqbal Q, Anjum A, Rehman MEU, Aijaz Z, et al. Pneumocystis jiroveci Pneumonia: A Review of Management in Human Immunodeficiency Virus (HIV) and Non-HIV Immunocompromised Patients. Avicenna J Med. 2023;13(1):23–34. Available from: https://doi.org/10.1055/s-0043-1764375

18. Tasaka S. Recent Advances in the Diagnosis and Management of Pneumocystis Pneumonia. Tuberc Respir Dis (Seoul). 2020;83(2):132–140. Available from: https://doi.org/10.4046/trd.2020.0015

19. Duan J, Gao J, Liu Q, Sun M, Liu Y, Tan Y, et al. Characteristics and Prognostic Factors of Non-HIV Immunocompromised Patients With Pneumocystis Pneumonia Diagnosed by Metagenomics Next-Generation Sequencing. Front Med (Lausanne). 2022;9:812698. Available from: https://doi.org/10.3389/fmed.2022.812698

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