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MINIREVIEWS

Pneumococcal disease in adult solid organ transplantation recipients

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Abstract

In solid organ transplant (SOT) recipients, *Streptococcus pneumoniae* can cause substantial morbidity and mortality ranging from non-invasive to invasive diseases, including pneumonia, bacteremia, and meningitis, with a risk of invasive pneumococcal disease 12 times higher than that observed in non-immunocompromised patients. Moreover, pneumococcal infection has been related to graft dysfunction. Several factors have been involved in the risk of pneumococcal disease in SOT recipients, such as type of transplant, time since transplantation, influenza activity, and nasopharyngeal colonization. Pneumococcal vaccination is recommended for all SOT recipients with 23-valent pneumococcal polysaccharides vaccine. Although immunological rate response is appropriate, it is lower than in the rest of the population, decreases with time, and its clinical efficacy is variable. Booster strategy with 7-valent pneumococcal conjugate vaccine has not shown benefit in this population. Despite its relevance, there are few studies focused on invasive pneumococcal disease in SOT recipients. Further studies addressing clinical, microbiological, and epidemiological data of pneumococcal disease in the transplant setting as well as new strategies for improving the protection of SOT recipients are warranted.

Key words: Transplantation; Pneumococcal infections; Pneumococcal serotypes; Nasopharyngeal carriage; Pneumococcal vaccine

Core tip: Streptococcus pneumoniae causes substantial morbidity and mortality in solid organ transplant (SOT) recipients, ranging from non-invasive to invasive diseases, with a 12-fold risk of invasive pneumococcal disease higher than in non-immunocompromised patients. Pneumococcal vaccination is recommended for all SOT recipients with 23-valent pneumococcal polysaccharides vaccine. Although immunological rate response is appropriate, it is lower than in the rest of the population, decreases with time, and its clinical

efficacy is variable. Booster strategy with 7-valent pneumococcal conjugate vaccine has not shown benefit in this population. Despite its relevance, robust evidence on pneumococcal disease in organ transplant recipients is lacking. New strategies for improving the protection of SOT recipients are warranted.

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INCIDENCE

Streptococcus pneumoniae (S. pneumoniae) is the cause of 3300 deaths every year in the United States, mainly among adults[1]. According to the United States Active Bacterial Core Surveillance Database of the Emerging Infections Program Network, in 2012 the incidence of invasive pneumococcal disease (IPD) ranged from 2.8 per 100000 persons aged 18-34 years to 29.6 per 100000 among those older than 65 years[1]. In the 2013 Annual Epidemiological Report of the European Centers for Disease Prevention and Control (ECDC) the incidence of IPD in Europe was even higher: 3.8 per 100000 persons per year[2]. Invasive pneumococcal disease is an important cause of illness in patients with certain underlying medical conditions[3] or demographic risk factors, including age < 2 or ⩾ 65 years, chronic diseases, alcohol abuse, smoking, and immunosuppressive conditions such as human immunodeficiency virus (HIV) infection[4], multiple myeloma, or solid organ transplantation (SOT)[5-10]. The disease rates for adults with high-risk factors can be more than 20 times that those for adults without high-risk medical conditions. Middle-aged patients with hematological cancer have a rate of IPD of 186 per 100000 persons per year during 2010 and HIV infected patients have a rate of IPD of 173 per 100000 persons per year[11].

In solid organ transplant recipients, *S. pneumoniae* can cause substantial morbidity and mortality, ranging from no invasive diseases such as otitis media, sinusitis, and non-bacteremic pneumonia to invasive diseases, including bacteremic pneumonia and meningitis[9]. Data from the literature on SOT recipients are referred almost exclusively to the most severe spectrum of disease. Invasive pneumococcal disease is defined as an isolation of *S. pneumoniae* from a sterile body fluid with a compatible clinical syndrome[12]. Sterile sites included blood, cerebrospinal fluid, peritoneal fluid, pleural fluid, or needle aspiration of a collection. Sputum or bronchoalveolar lavage isolates are not considered sterile-site isolates in some studies[13]. The risk of developing invasive pneumococcal disease in these patients has been estimated in studies carried out in the 70s[14], 80s[15], and 90s[16] to be 2800 per 100000 patient-years in a cohort of kidney transplant recipients[14], 3600 per 100000 patient-years in heart transplant recipients[15], and 2270 per 100000 patient-years in lung transplant recipients[16]. The first two studies were conducted in the pre-vaccine era, justifying higher incidence rates, while in the latter all lung transplant recipients had received pneumococcal vaccine before transplantation. Moreover, in one of the studies most of the kidney recipients were splenectomized, due to the belief at that time that such procedure prolonged graft survival, thus increasing expected IPD cases[14]. However, it is difficult to compare the findings of these different studies, due to the disparity of vaccination rates, types of organ transplantation, and immunosuppression protocols according to the time when the studies were carried out. A recent study prospectively determined the incidence of IPD in a population of adult SOT recipients over a period of almost 10 years, with an incidence of 146 per 100000 persons per year, 12.8 times greater than that in the general population. Specific incidences for kidney, lung, and liver transplant recipients were 104, 239, and 354 per 100000 transplant recipients per year, respectively, compared to 11.5 cases per 100000 person-years in the general population. Interestingly, there were no cases of IPD in heart and pancreas transplant recipients[9].

Non-bacteremic pneumococcal pneumonia is the most relevant non-IPD among SOT recipients, due to its morbidity and mortality. *S. pneumoniae* is the second or third leading cause of late community-acquired pneumonia in solid organ transplantation[17-21]. As in other infections, pneumococcal pneumonia incidence depends on the type of SOT, being more frequent in lung transplant recipients (3262 per 100000 persons-year) followed by kidney (344 per 100000 persons-year) and liver recipients (304 per 100000 persons-year)[9].

RISK FACTORS OF PNEUMOCOCCAL DISEASE

Several risk factors of pneumococcal disease in SOT recipients have been described. The type of organ transplanted is one of the most important, as previously stated. Liver transplant recipients have an increased risk of IPD, while lung recipients have the highest rates of pneumococcal pneumonia, followed by heart and kidney recipients[9,16,21].

Time since transplantation is another factor to be considered. The median time since transplantation to the onset of pneumococcal infection is 1.3 to 2.7 years[9,16,21]. Although Amber *et al*[15], in a study carried out in 5 heart recipients, found that the median time for IPD was 58 d (range 1-5 mo), in

most of the studies pneumococcal disease occurs after the first 4 to 6 mo from the transplantation[9,16]. In a prospective multicenter study carried out in Canada, 57% of the cases were diagnosed during the first three years since transplantation, while one fifth of them occurred after the first 10 years of the transplant[9].

Although the sizes of most of the studies publishes are underpowered to establish statistical associations, the type of immunosuppressors has not been related to an increased risk of pneumococcal disease[9,14-16]. Neither has been found an increased risk of hospital mortality in patients with classic risk factors in the general population, as age, diabetes mellitus, chronic renal disease, or splenectomy[9]. Probably, the small number of the studies in the literature in this group of immunosuppressed patients and their heterogeneity do not allow drawing appropriate conclusions.

The role of universal prophylaxis with trimethoprim-sulfamethoxazole (TMP/SMX) in the prevention of pneumococcal disease in SOT recipients has not been established. Use of TMP/SMX prophylaxis at the moment of pneumococcal disease diagnosis is common among SOT recipients, with a frequency that ranges from 14% to 100% of the cases. However, the rate of TMP/SMX resistant isolates in these patients is high (66% to 71%)[9,16]. This high rate of resistance to TMP/SMX invalidates this measure to prevent pneumococcal disease.

Nasopharyngeal colonization is a preliminary step in the development of pneumococcal disease, with transmission only coming from other human carriers[22]. Pneumococcal colonization has been mainly studied in children, as the highest rates of colonization are found during childhood. As children grow older, the prevalence of pneumococcal carriage decreases, and the distribution of colonizing serotypes changes. With the introduction of the 7-valent pneumococcal conjugate vaccine (PCV7) the colonization rate in children has been reduced from 50%-70%[23-26] to 21%-33% in the United States and Europe[27-30]. Pneumococcal colonization studies carried out in children have increased the knowledge about the rate of colonization, the circulating serotypes, the serotypes (mostly encapsulated) related to invasive disease, the expected pattern of resistance and, specially, the effectiveness of the recently introduced new pneumococcal vaccines, offering a better understanding of the pneumococcal disease in the children population[2,31-33].

There are very few data regarding *S. pneumoniae* nasopharyngeal carriage in healthy adults, showing colonization rates of 4%-13%[25,34], depending on the geographic area of the population studied[23,25,26,35-37], and the presence of underlying diseases. Patients with asthma, mainly treated with inhaled corticosteroids, have a higher risk of *S. pneumoniae* colonization than the healthy population[6,38-40]. In immunosuppressed patients, the information available is scarce. In HIV-infected adults, the frequency of pneumococcal colonization ranges from 3.4% in United States, to 17% in Brazil and 52% in Malawi[34,41,42]. No information of pneumococcal colonization in SOT recipients is available.

Influenza activity has been associated with significant increases in the incidence of invasive pneumococcal pneumonia, both in children and adults. The association was more pronounced among younger adults without co-morbidities[43]. In non-immunocompromised patients, influenza is associated with the greatest increase in the incidence of bacteremic pneumococcal pneumonia caused by serotypes with lower invasive potential. The importance of influenza for adult bacteremic pneumococcal pneumonia varies by serotype and host co-morbidity[44]. Although there are no studies that address the impact of influenza activity in the incidence of IPD in the transplant setting, it is plausible that there might be a relationship between both diseases.

One of the most important virulence factors of *S. pneumoniae* is the polysaccharide capsule. Chemical and antigenic differences in this capsule result in more than 90 different capsular types or serotypes, 20 of which cause the majority of invasive disease[45,46]. According to the results of a meta-analysis of adults with pneumococcal bacteremic pneumonia, the risk of death varies with the serotype and is stable among studies across time and in diverse geographic locations. Patients with pneumonia caused by serotypes 3, 6A, 6B, 9N, and 19F died more frequently than those caused by serotype 14. In contrast, patients infected with serotypes 1, 7F, and 8 were significantly less likely to die than those infected with serotype 14[31]. In a study carried out in Spain, during 2012, the most frequent serotypes linked to IPD in the general population were 1, 3, 7F, 19A, 12F, 14, 22F, 24F, 8, 9A, 4, 10A, and 11A[46]. In Europe, in adults older 15 years old, the ten most common serotypes of IPD in 2011 ordered by frequency were 7F, 19A, 3, 1, 22F, 8, 14, 12F, 6C and 4, accounting for 61.5% of the typed isolates[2].

In SOT recipients, serotypes distribution in invasive pneumococcal disease is slightly different from general population. Kumar *et al*[9] reported that the most frequent serotypes in 21 cases of recent cases of IPD were 23F (4/21, 19%), 22F (3/21, 14.2%) and 19F (2/21, 9.5%), followed by at least one case of 4, 6A, 6B, 8, 9V, 11, 13, 14, 18C and 35V. De Bruyn *et al*[16] also reported serotype 23F as the most frequent in the IPD occurring in lung transplant recipients (27.2%), followed by 19A (18.1%), 6A/B (18.1%), and at least one case of 3, 4 and 9V. In these more recent studies, serotype of dead patients because of IPD was not specified.

Table 1 Outcome of invasive pneumococcal disease in solid organ transplantation recipients

Ref.	*n*	Inclusion period	Organ	Time since transplant median (range)	Type of IPD	Prior vaccination	Most frequent isolated serotypes	Graft dysfunction/loss	Mortality
Linnemann *et al*[14]	12	1971-1977	Kidney	No data	Pneumonia: 83% Bacteremia: 41% Meningitis: 16%	No	8, 9, 12, 24	75%/22.2%	8.30% (1/12)
Amber *et al*[15]	5	1985-1987	Heart	0.15 yr (1.2-4.4 mo)	Pneumonia: 80% Bacteremia: 20%	No	3	20%/No data	0%
de Bruyn *et al*[16]	14	1992-2003	Lung	1.3 yr (9.6 mo-2.3 yr)	Pneumonia: 78% Bacteremia: 21%	100%	23F, 19A, 6	No data	7.10% (1/14)
Kumar *et al*[9]	21	1995-2004	Kidney: 11 Liver: 9 Lung: 1	2.7 yr (1.3 mo-23.8 yr)	Pneumonia: 57% Bacteremia: 33% Peritonitis: 5% Parotitis: 5%	23.80%	23F, 22F, 19F	No data	28.60% (6/21)

IPD: Invasive pneumococcal disease.

CLINICAL MANIFESTATIONS

The clinical features of invasive pneumococcal disease in SOT recipients are similar to those of the general population. Bacteremic pneumococcal pneumonia is the most frequent manifestation followed by primary bacteremia and meningitis[9,14-16]. Kumar *et al*[9] reported an incidence of 90.5% cases of bacteremia (19/21), 57.1% cases of pneumonia (12/21), and 33.3% cases of primary bacteremia (7/21), with no cases of meningitis. These proportions were similar to those described by de Bruyn *et al*[16] and Linnemann *et al*[14], reported 83.3% of pneumonia, 41.6% of bacteremia and 16.6% of meningitis in kidney recipients during the 80s. In the general population in United States, the frequency of bacteremic pneumonia is 69.1%, primary bacteremia 16.8% and meningitis 7%[1]. By contrast, in the European general population, there is a lower rate of bacteremic pneumonia (48%), with higher rate of primary bacteremia (29%), and meningitis (18%)[33]. Other rare manifestations of IPD has been previously described in case reports or case series of SOT recipients, including peritonitis or parotitis[9]; endocarditis, spondylitis, and muscle abscess[47]; and necrotizing fasciitis[48]. Despite its low frequency, reports of sporadic cases highlight an important clinical aspect: *S. pneumoniae* may cause suppurate infection in virtually any anatomic location, with or without prior detected bacteremia.

IMPACT ON PATIENT AND GRAFT SURVIVAL

Invasive pneumococcal disease results in significant morbidity and mortality. Kumar *et al*[9] reported an in-hospital mortality due to IPD in SOT recipients of 28.6% (6/21), 66.7% (4/6) of them directly attributable to pneumococcal infection. Although they did not find statistically differences of mortality among SOT recipients and non-immunosuppressed patients (28.6% *vs* 17.8%), this mortality is higher than that reported in most of the studies carried out in general populations, where the mortality due to pneumococcal bacteremia ranges from 12% to 17%[49,50].

Length of hospitalization is also higher in SOT recipients (16.2 d *vs* 11.6 d), probably related to long antibiotics course and complications[9,16,50]. de Bruyn *et al*[16] reported more severe complications, requiring mechanical ventilation, in the group of lung transplant recipients who developed bacteremic pneumococcal pneumonia compared with those with non-bacteremic pneumococcal pneumonia. Allograft dysfunction has been associated to pneumococcal infection, as observed with other infections in SOT recipients[51]. Linnemann *et al*[14] described a rate of allograft dysfunction in renal transplant recipients with IPD as high as 75% (9/12), with a 22% of cases presenting definitive graft loss (2/9). Amber *et al*[15] also reported a 20% (1/5) of allograft dysfunction after IPD, in addition to two cases of graft dysfunction treated with increased immunosuppression and complicated with IPD within 20 d. However, graft dysfunction has not been analyzed in the most recent studies of IPD in SOT recipients[9,16]. Therefore, data available of graft dysfunction are referred exclusively to older studies carried out in heart and kidney transplant recipients and on a small number of patients (Table 1). New prospective studies are required to confirm these data and to analyze the risk of rejection and graft dysfunction in SOT recipients after an episode of IPD.

VACCINATION

Knowledge of the most invasive serotypes allowed the development of the first pneumococcal vaccine. In 1983, a 23-valent pneumococcal polysaccharide vaccine (PPV23) was approved, expanding serotype coverage to more than 85% of the organisms causing IPD[52]. This vaccine induces a humoral immune response through the production of specific antibodies, but do not prompt immunological

memory. This aspect, added to the fact that PPV23 induced poor T-cell-independent immunogenicity in infants led to development of the pneumococcal conjugate vaccine[52]. The pneumococcal conjugate vaccine consists of capsular polysaccharides from the most common serotypes that cause IPD along with a carrier protein, and induce a T-cell-dependent immune response, so that they are able to produce immunological memory and greater immunogenic response than that produced by the PPV23[53]. Another advantage of pneumococcal conjugate vaccine is that stimulates mucosal immunity, resulting in decreased naso-pharynx colonization and also exhibits secondary protection of unvaccinated individuals. Pneumococcal conjugate vaccine (PCV) was initially approved in children less than two years while PPV23 was recommended for children over two years, adults and immunocompromised patients, including SOT recipients.

The first PCV7 was licensed in the United States in 2000 and introduced in Europe in 2001. This vaccine included capsular polysaccharides of serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F, representing approximately 80%-90% of IPD in children. With serotype shifts resulting from vaccine pressure, the protective coverage of PCV7 was reduced, as this vaccine did not include serotypes 1, 3, and 5, which are common in Europe, Asia, and Africa. Therefore, a 13-valent conjugate vaccine (PCV13) including serotypes 1, 3, 5, 6A, 7F, and 19A, was licensed in 2009 in Europe. In 2010, the theoretical vaccine preventable proportion of cases using PCV7, PCV10 and PCV13 in children under five years was 19.2%, 46.1% and 73.1% respectively[33].

The use of pneumococcal vaccination determined a reduction in the number of cases of invasive and non-invasive pneumococcal disease in children and adults. Several randomized trials and meta-analyses concluded that PPV23 prevents pneumococcal disease in adult population[54-56]. Other studies suggest that PPV23 protects against invasive infection but not from non bacteremic pneumococcal pneumonia[56-58] and it did not affect survival[54]. However, in most of these studies the etiology of community-acquired pneumonia was not confirmed, assuming the expected higher frequency of pneumococcal etiology. In general, studies with more specific endpoints as IPD caused by vaccine serotypes have been more likely to demonstrate efficacy than studies with less specific ones.

In immunosuppressed population, data are scarce and heterogeneous. In SOT recipients, vaccine efficacy is derived from studies conducted mostly in kidney transplant recipients[59-65] (Table 2), with less information available in heart[15,66,67] and liver transplant recipients[68] (Table 3). Moreover, most studies of vaccination in SOT were performed with the old 14-serotypes polysaccharide vaccine (previous to the introduction of the PPV23 in 1980s) and with different methods for detecting immunity, such as radioimmunoassay. Nevertheless, practically all studies agrees that pneumococcal vaccine in SOT recipients is effective, but the immune response is weaker than in healthy controls and that there is a greater loss of antibodies over time, especially in the first months after the transplant[59-62,64,65]. Studies carried out in SOT recipients with the PPV23 vaccine yield similar conclusions[66,68-70]: there was an adequate post-vaccine response but the antibody titers decreased from the sixth month after vaccination[68,70]. This decrease in the geometric mean titer of antibodies also occurs after the naturally acquired pneumococcal immunity after transplantation[15]. Interestingly, Blumberg *et al*[67] evaluated the impact of prior antibody titers and its relationship with the elicited immune response. In this study, patients with previous antibody titers, although low, obtained better post-vaccine titers after receiving a second vaccine dose (Tables 2 and 3). It is important to emphasize that in all the studies regarding pneumococcal vaccination in SOT recipients, the vaccine was safe, regardless of its effectiveness.

Globally, the knowledge gained from the use of the polysaccharide vaccine in adults reveals that new vaccine strategies are needed to increase vaccine efficacy, especially in vulnerable populations, such as the elderly and immunocompromised patients. In this sense, testing the hypothetical usefulness of the conjugate vaccine (typically used in children) in adult population was performed, supported by the previously discussed benefits. A single study carried out in HIV-infected patients, most of them without antiretroviral therapy, reported protection against pneumococcal disease with PCV7, but not with the polysaccharide vaccine.

Based on these observations, in 2012, the Advisory Committee on Immunization Practices (ACIP) recommended routine PCV13 use for adults aged $\geqslant$ 19 years with immune compromise conditions, including SOT recipients, functional or anatomic asplenia, cerebrospinal fluid leaks, or cochlear implants. This vaccine should be administered to eligible adults but in addition to PPV23, the vaccine currently recommended for these groups of adults[71,72] and SOT recipients, specifically[73,74]. This strategy appears to be a cost-effective vaccine policy[75].

However, according to the 2013 ECDC surveillance report, the emergence of non-vaccine serotypes remains an important issue, and continued monitoring in Europe is essential for assessing interventions and informing the development of new vaccines[2]. This might be especially relevant in the transplant setting. Immunosuppressed patients can have a different serotype distribution than the general population. In a recent study, carried out in Spain, serotypes not included in the PCV13 and

Table 2 Pneumococcal vaccination studies in kidney transplantation in adult recipients

Ref.	*N*	Time since transplant	Vaccine	Technique	Response to immunization	Long term immune response
Silberman *et al*[59]	27 KT *vs* 24 healthy adults	7-108 mo	14-valent	Indirect hemagglutination	4-fold increase in titers, equivalent to controls	Not studied
Marrie *et al*[60]	63 KT *vs* 8 healthy adults	3-99 mo	14-valent	RIA	2.8-fold increase in titers in KT *vs* 3.4-fold in controls	GMT in KT: 872 ng N/mL post-vaccine 659 ng N/mL at 12 mo
Cosio *et al*[61]	25 KT (14 asplenia) *vs* 14 healthy adults	3-118 mo	14-valent	RIA	2-fold increase in titers in 93% of 14 healthy adults *vs* 78% of 14 splenectomized KT and 55% of 11 non-splenectomized KT patients	Not studied
Linneman *et al*[62,63]	104 KT (79 asplenia) *vs* 33 patients in hemodialysis	No data	14-valent	RIA	1.4-fold increase in antibody titers: 91%GMT post-vaccine with lower response in splenectomized KT *vs* non-splenectomized KT patients (394 *vs* 626 ng N/mL, $P < 0.05$) GMT post-vaccine with lower response in KT patients before 6 mo after transplant vs hemodialysis patients (303 *vs* 592 ng N/mL, $P < 0.05$)	GMT at 24 mo in 33 KT: 932 ng N/mL post-vaccine 385 ng N/mL at 24 mo 536 ng N/mL at revaccination
Arnold *et al*[64]	75 KT (32 asplenia) *vs* 60 healthy controls	> 12 mo	14-valent	Serum opsonizing antibody	2-fold increase in titers to serotypes 12F and 14 No differences in splenectomized *vs* non-splenectomized KT recipients	Not studied
Rytel *et al*[65]	61 KT (57 asplenia) *vs* 23 patients in dialysis *vs* 9 healthy controls	> 6 mo	14-valent	RIA	Equivalent protective GMT titers *vs* controls	Equivalent at 1, 2, and 3.5 yr *vs* controls
Kazancioglu *et al*[69]	21 KT *vs* 25 healthy controls	> 2 mo	PPV23	ELISA	Protective response to vaccination (40% increases in the antibody concentration) in 95.2% of KT at 1.5 and 3 mo after vaccination	Not studied
Kumar *et al*[78,79]	30 KT (PPV23) *vs* 30 KT (PCV7)	3 mo-3 yr	PPV23 *vs* PCV7	ELISA, OPA	Response to at least 1 serotype: no significant differences in antibody titers between PPV23 and PVC7, both using ELISA (53.3% *vs* 73.3%) and OPA (83.3% *vs* 80%)	Vaccine responses decline significantly after 3 yr and conjugate vaccine does not improve the durability of response

KT: Kidney transplantation; PPV23: 23-valent pneumococcal polysaccharide vaccine; PCV7: 7-valent pneumococcal conjugate vaccine; RIA: Radioimmunoassay; ELISA: Enzyme-Linked ImmunoSorbent Assay; OPA: Opsonophagocytic assay; GMT: Geometric Mean Titer.

PPV23 formulations were more frequently isolated in patients with IPD and cardio-respiratory co-morbidities or immunosuppression, including SOT recipients. Indeed, three serotypes (10A, 11A, and 33F), not included in the PCV13 formulation, were the most frequently isolated in immunocompromised patients with IPD, although their prevalence in the complete cohort was low[8]. According to Kumar *et al*[9], only 23.8% of the SOT recipients with IPD had been previously vaccinated with PPV23. In this study, 65% of transplant recipients had disease due to pneumococcus serotypes included in the PCV13 and 85% of them had disease due to serotypes included in the PPV23[9].

Clinical failure of pneumococcal vaccine is common in the transplant setting. Thus, 24% to 100% of the SOT recipients with pneumococcal disease had being vaccinated[9,16]. One possible explanation could be the different pneumococcal serotypes distribution observed in the transplant setting and the proportion of serotypes not included in the pneumococcal vaccine. Other aspect to consider is the reduction in the effectiveness of pre-transplant pneumococcal vaccine in the context of end-organ disease previous to the transplant, as kidney, liver or heart disease, and in the post-transplant due to the use of immunosuppressors necessary to prevent graft rejection, as observed in a study, where all SOT recipients with IPD had received the PPV23 vaccination with all the serotypes producing pneumococcal disease covered by the vaccine[16]. The required post-transplant immunosuppression may cause progressive decrease of the levels of antibody previously achieved, like other immunizations in SOT recipients, as influenza[76].

New strategies have been proposed to enhance the immunogenic response and clinical efficacy obtained by PPV23 in SOT recipients, which include revaccination, use of pneumococcal conjugate vaccine, or "booster" strategy. Revaccination with polysaccharide antigens does not elicit a suitable

Table 3 Pneumococcal vaccination studies in heart and liver transplantation in adult recipients

Ref.	*n*	Type and time since transplant	Vaccine	Technique	Response to immunization	Long term immune response
McCashland *et al*[68]	25 LT *vs* 13 healthy controls	LT 1 - 6 mo	PPV23	ELISA	Pneumococcal antibody levels were significantly increased over baseline by 1 mo after vaccination in both groups	At 6th mo: antibody levels declined faster in patients than in control subjects
Amber *et al*[15]	6 HT before and after transplantation	HT 0.6 - 5.3 mo	Unvaccinated	RIA	Protective antibody titers to 12 pneumococcal serotypes contained in PPV23 in a mean of 8.7 ± 1.2 serotypes before transplantation *vs* 6.5 ± 1.4 serotypes after transplantation ($P < 0.05$)	Not studied
Dengler *et al*[66]	16 HT *vs* 23 healthy controls	HT > 12 mo	PPV23	ELISA	Protective post-vaccine antibody titers (> 1000 U/mL): 94% in HT recipients *vs* 100% in controls	Not studied
Blumberg *et al*[67]	35 HT *vs* 35 healthy controls. Group 2 ($n = 21$), vaccinated before this study The HT patients were classified as: Group 1 ($n = 11$), no vaccinated before this study No data about previous vaccine ($n = 2$)	HT 55 - 122 mo	PPV23	ELISA	Post-vaccine antibody titers were higher in group 2 than in group 1 for all pneumococcal serotypes ($P < 0.05$ for all serotypes, except 3)	Detectable antibody titers at 24 mo (only 7 available patients) in 50% to serotypes 19F and 23F and in 80% to serotype 3

LT: Liver transplantation; HT: Heart transplantation; PPV23: 23-valent pneumococcal polysaccharide vaccine; ELISA: Enzyme-Linked ImmunoSorbent Assay; RIA: Radioimmunoassay.

memory response in healthy people[77] and kidney recipients respond less vigorously to revaccination than to primary immunization[63]. Trials comparing PCV7 with PPV23 in renal transplant recipients have not succeeded in achieving differences in immunogenicity between these vaccines[78,79]. Furthermore, the recommendation made by the ACIP of a prime-boost strategy (PCV13 followed by PPV23 8 wk later) in adult > 50 years old and in immunocompromised patients has been evaluated in SOT recipients with unfavorable results. Kumar *et al*[80]. randomized 130 adult liver transplant recipients to receive either PCV7 followed by a PPV23 booster 8 wk later (the "primed" group) or placebo followed by a standard single dose of PPV23 (the "unprimed" group, as usual practice). There was no difference in immune response between the two groups More recently, Tobudic *et al*[81] randomized 80 kidney transplants recipients to received either PCV7 or PPV23 followed by PPV23 the following year. There was no benefit in either of the sequential regimens when compared with single-dose PPV23 vaccination as recommended by the guidelines.

CONCLUSION

S. pneumoniae can cause substantial morbidity and mortality in SOT recipients, ranging from non-invasive to invasive diseases, including bacteremic pneumonia and meningitis, with a 12-fold risk of IPD higher than in non-immunocompromised patients. Despite its relevance, there are few studies focused on IPD in SOT recipients. Pneumococcal vaccination is recommended for all SOT recipients with PPV23. Although immunological rate response is appropriate, it is lower than that in the rest of the population, decreases with time, and its clinical efficacy is variable. Booster strategy with PCV7 has not shown benefit in this population. Further studies addressing clinical, microbiological, and epidemiological data of pneumococcal disease in the transplant setting as well as new strategies for improving the protection of SOT recipients are warranted.

REFERENCES

1 **Centers for Disease Control and Prevention (CDC).** Active Bacterial Core Surveillance Report, Emerging Infections Program Network, Streptococcus pneumoniae, 2010. USA: CDC, 2011

2 **European Centre for Disease Prevention and Control.** Annual Epidemiological Report 2013. Reporting on 2011 surveillance data and 2012 epidemic intelligence data. Stockholm: ECDC, 2013

3 **Lipsky BA**, Boyko EJ, Inui TS, Koepsell TD. Risk factors for acquiring pneumococcal infections. *Arch Intern Med* 1986; **146**: 2179-2185 [PMID: 3778047 DOI: 10.1001/archinte.1986.00360230105016]

4 **McEllistrem MC**, Mendelsohn AB, Pass MA, Elliott JA, Whitney CG, Kolano JA, Harrison LH. Recurrent invasive pneumococcal disease in individuals with human immunodeficiency virus infection. *J Infect Dis* 2002; **185**: 1364-1368 [PMID: 12001059 DOI: 10.1086/339882]

5 **Gentile JH**, Sparo MD, Mercapide ME, Luna CM. Adult bacteremic pneumococcal pneumonia acquired in the community. A prospective study on 101 patients. *Medicina* (B Aires) 2003; **63**: 9-14 [PMID: 12673954]

6 **Talbot TR**, Hartert TV, Mitchel E, Halasa NB, Arbogast PG, Poehling KA, Schaffner W, Craig AS, Griffin MR. Asthma as a risk factor for invasive pneumococcal disease. *N Engl J Med* 2005; **352**: 2082-2090 [PMID: 15901861 DOI: 10.1056/NEJMoa044113]

7 **Chi RC**, Jackson LA, Neuzil KM. Characteristics and outcomes of

older adults with community-acquired pneumococcal bacteremia. *J Am Geriatr Soc* 2006; **54**: 115-120 [PMID: 16420207 DOI: 10.1111/j.1532-5415.2005.00528.x]

8 **Luján M**, Burgos J, Gallego M, Falcó V, Bermudo G, Planes A, Fontanals D, Peghin M, Monsó E, Rello J. Effects of immunocompromise and comorbidities on pneumococcal serotypes causing invasive respiratory infection in adults: implications for vaccine strategies. *Clin Infect Dis* 2013; **57**: 1722-1730 [PMID: 24065334 DOI: 10.1093/cid/cit640]

9 **Kumar D**, Humar A, Plevneshi A, Green K, Prasad GV, Siegal D, McGeer A. Invasive pneumococcal disease in solid organ transplant recipients--10-year prospective population surveillance. *Am J Transplant* 2007; **7**: 1209-1214 [PMID: 17286615 DOI: 10.1111/j.1600-6143.2006.01705.x]

10 **Cordero E**, Pachón J, Rivero A, Girón JA, Gómez-Mateos J, Merino MD, Torres-Tortosa M, González-Serrano M, Aliaga L, Collado A, Hernández-Quero J, Barrera A, Nuño E. Community-acquired bacterial pneumonia in human immunodeficiency virus-infected patients: validation of severity criteria. The Grupo Andaluz para el Estudio de las Enfermedades Infecciosas. *Am J Respir Crit Care Med* 2000; **162**: 2063-2068 [PMID: 11112115 DOI: 10.1164/ajrccm.162.6.9910104]

11 **Centers for Disease Control and Prevention (CDC).** Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine for adults with immunocompromising conditions: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep* 2012; **61**: 816-819 [PMID: 23051612]

12 Decision 2002/253/EC laying down case definitions for reporting communicable diseases to the Community network under Decision No 2119/98/EC of the European Parliament and of the Council. *OJEU* 2008; **159**: 46-90

13 **Gill VJ,** Fedorko DP, Witebsky FG. The clinician and the microbiology laboratory. In: Principles and Practice of Infectious Diseases. Mandel GL, Bennett JE, Dolin R, editors. Churchill: Livingstone; 2005: 203-241

14 **Linnemann CC**, First MR. Risk of pneumococcal infections in renal transplant patients. *JAMA* 1979; **241**: 2619-2621 [PMID: 374767 DOI: 10.1001/jama.1979.03290500027016]

15 **Amber IJ**, Gilbert EM, Schiffman G, Jacobson JA. Increased risk of pneumococcal infections in cardiac transplant recipients. *Transplantation* 1990; **49**: 122-125 [PMID: 2301002 DOI: 10.1097/00007890-199001000-00027]

16 **de Bruyn G**, Whelan TP, Mulligan MS, Raghu G, Limaye AP. Invasive pneumococcal infections in adult lung transplant recipients. *Am J Transplant* 2004; **4**: 1366-1371 [PMID: 15268742 DOI: 10.1111/j.1600-6143.2004.00512.x]

17 **Eyüboğlu FÖ,** Küpeli E, Bozbaş SS, Ozen ZE, Akkurt ES, Aydoğan C, Ulubay G, Akçay S, Haberal M. Evaluation of pulmonary infections in solid organ transplant patients: 12 years of experience. *Transplant Proc* 2013; **45**: 3458-3461 [PMID: 24314931 DOI: 10.1016/j.transproceed.2013.09.024]

18 **Cervera C**, Agustí C, Angeles Marcos M, Pumarola T, Cofán F, Navasa M, Pérez-Villa F, Torres A, Moreno A. Microbiologic features and outcome of pneumonia in transplanted patients. *Diagn Microbiol Infect Dis* 2006; **55**: 47-54 [PMID: 16500066 DOI: 10.1016/j.diagmicrobio.2005.10.014]

19 **Cisneros JM**, Muñoz P, Torre-Cisneros J, Gurgui M, Rodriguez-Hernandez MJ, Aguado JM, Echaniz A. Pneumonia after heart transplantation: a multi-institutional study. Spanish Transplantation Infection Study Group. *Clin Infect Dis* 1998; **27**: 324-331 [PMID: 9709883 DOI: 10.1086/514649]

20 **Fishman JA**, Rubin RH. Infection in organ-transplant recipients. *N Engl J Med* 1998; **338**: 1741-1751 [PMID: 9624195 DOI: 10.1056/NEJM199806113382407]

21 **Giannella M**, Muñoz P, Alarcón JM, Mularoni A, Grossi P, Bouza E. Pneumonia in solid organ transplant recipients: a prospective multicenter study. *Transpl Infect Dis* 2014; **16**: 232-241 [PMID: 24593292 DOI: 10.1111/tid.12193]

22 **van der Poll T**, Opal SM. Pathogenesis, treatment, and prevention of pneumococcal pneumonia. *Lancet* 2009; **374**: 1543-1556 [PMID: 19880020 DOI: 10.1016/S0140-6736(09)61114-4]

23 **Bogaert D**, De Groot R, Hermans PW. Streptococcus pneumoniae colonisation: the key to pneumococcal disease. *Lancet Infect Dis* 2004; **4**: 144-154 [PMID: 14998500 DOI: 10.1016/S1473-3099(04)00938-7]

24 **Greenberg D**, Broides A, Blancovich I, Peled N, Givon-Lavi N, Dagan R. Relative importance of nasopharyngeal versus oropharyngeal sampling for isolation of Streptococcus pneumoniae and Haemophilus influenzae from healthy and sick individuals varies with age. *J Clin Microbiol* 2004; **42**: 4604-4609 [PMID: 15472316 DOI: 10.1128/JCM.42.10.4604-4609.2004]

25 **Regev-Yochay G**, Raz M, Dagan R, Porat N, Shainberg B, Pinco E, Keller N, Rubinstein E. Nasopharyngeal carriage of Streptococcus pneumoniae by adults and children in community and family settings. *Clin Infect Dis* 2004; **38**: 632-639 [PMID: 14986245 DOI: 10.1086/381547]

26 **Neves FP**, Pinto TC, Corrêa MA, dos Anjos Barreto R, de Souza Gouveia Moreira L, Rodrigues HG, Cardoso CA, Barros RR, Teixeira LM. Nasopharyngeal carriage, serotype distribution and antimicrobial resistance of Streptococcus pneumoniae among children from Brazil before the introduction of the 10-valent conjugate vaccine. *BMC Infect Dis* 2013; **13**: 318 [PMID: 23849314 DOI: 10.1186/1471-2334-13-318]

27 **Özdemir H**, Çiftçi E, Durmaz R, Güriz H, Aysev AD, Karbuz A, Gökdemir R, Acar B, Nar-Ötgün S, Ertek M, Köse SK, İnce E. Risk factors for nasopharyngeal carriage of Streptococcus pneumoniae in healthy Turkish children after the addition of heptavalent pneumococcal conjugate vaccine (PCV7) to the national vaccine schedule. *Turk J Pediatr* 2013; **55**: 575-583 [PMID: 24577974 DOI: 10.1007/s00431-013-2156-7]

28 **Wroe PC**, Lee GM, Finkelstein JA, Pelton SI, Hanage WP, Lipsitch M, Stevenson AE, Rifas-Shiman SL, Kleinman K, Dutta-Linn MM, Hinrichsen VL, Lakoma M, Huang SS. Pneumococcal carriage and antibiotic resistance in young children before 13-valent conjugate vaccine. *Pediatr Infect Dis J* 2012; **31**: 249-254 [PMID: 22173142 DOI: 10.1097/INF.0b013e31824214ac]

29 **García-Vera C**, Ruiz Andrés MÁ, Arana Navarro T, Moneo Hernández I, Castillo Laita JA, Macipe Costa R, Revillo Pinilla MJ. [Nasopharyngeal carriage of pneumococcal serotypes in healthy pre-school aged children after 7-valent pneumococcal vaccine]. *Med Clin* (Barc) 2011; **137**: 1-7 [PMID: 21514939 DOI: 10.1016/j.medcli.2010.09.051]

30 **Obando I**, Sánchez-Tatay D, Molinos-Quintana A, Delgado-Pecellin I, Porras A, Morillo-Gutiérrez B, Fenoll A, Lirola MJ. [Epidemiology of nasopharyngeal carriage of Streptococcus pneumoniae in children & lt; 6 years old in Seville]. *Enferm Infecc Microbiol Clin* 2011; **29**: 581-586 [PMID: 21821320 DOI: 10.1016/j.eimc.2011.05.010]

31 **Weinberger DM**, Harboe ZB, Sanders EA, Ndiritu M, Klugman KP, Rückinger S, Dagan R, Adegbola R, Cutts F, Johnson HL, O' Brien KL, Scott JA, Lipsitch M. Association of serotype with risk of death due to pneumococcal pneumonia: a meta-analysis. *Clin Infect Dis* 2010; **51**: 692-699 [PMID: 20715907 DOI: 10.1086/655828]

32 **Brueggemann AB**, Peto TE, Crook DW, Butler JC, Kristinsson KG, Spratt BG. Temporal and geographic stability of the serogroup-specific invasive disease potential of Streptococcus pneumoniae in children. *J Infect Dis* 2004; **190**: 1203-1211 [PMID: 15346329 DOI: 10.1086/423820]

33 **European Centre for Disease Prevention and Control.** Surveillance of invasive pneumococcal disease in Europe, 2010. Stockholm: ECDC, 2012

34 **Glennie SJ**, Banda D, Gould K, Hinds J, Kamngona A, Everett DD, Williams NA, Heyderman RS. Defective pneumococcal-specific Th1 responses in HIV-infected adults precedes a loss of control of pneumococcal colonization. *Clin Infect Dis* 2013; **56**: 291-299 [PMID: 23024291 DOI: 10.1093/cid/cis842]

35 **Farida H**, Severin JA, Gasem MH, Keuter M, Wahyono H, van den Broek P, Hermans PW, Verbrugh HA. Nasopharyngeal carriage of Streptococcus pneumonia in pneumonia-prone age groups in Semarang, Java Island, Indonesia. *PLoS One* 2014; **9**: e87431

[PMID: 24498104 DOI: 10.1371/journal.pone.0087431]
36 **Park SY**, Moore MR, Bruden DL, Hyde TB, Reasonover AL, Harker-Jones M, Rudolph KM, Hurlburt DA, Parks DJ, Parkinson AJ, Schuchat A, Hennessy TW. Impact of conjugate vaccine on transmission of antimicrobial-resistant Streptococcus pneumoniae among Alaskan children. *Pediatr Infect Dis J* 2008; **27**: 335-340 [PMID: 18316986 DOI: 10.1097/INF.0b013e318161434d]
37 **Mehr S**, Wood N. Streptococcus pneumoniae--a review of carriage, infection, serotype replacement and vaccination. *Paediatr Respir Rev* 2012; **13**: 258-264 [PMID: 23069126 DOI: 10.1016/j.prrv.2011.12.001]
38 **Cardozo DM**, Nascimento-Carvalho CM, Andrade AL, Silvany-Neto AM, Daltro CH, Brandão MA, Brandão AP, Brandileone MC. Prevalence and risk factors for nasopharyngeal carriage of Streptococcus pneumoniae among adolescents. *J Med Microbiol* 2008; **57**: 185-189 [PMID: 18201984 DOI: 10.1099/jmm.0.47470-0]
39 **Jounio U**, Juvonen R, Bloigu A, Silvennoinen-Kassinen S, Kaijalainen T, Kauma H, Peitso A, Saukkoriipi A, Vainio O, Harju T, Leinonen M. Pneumococcal carriage is more common in asthmatic than in non-asthmatic young men. *Clin Respir J* 2010; **4**: 222-229 [PMID: 20887345 DOI: 10.1111/j.1752-699X.2009.00179.x]
40 **Zhang L**, Prietsch SO, Mendes AP, Von Groll A, Rocha GP, Carrion L, Da Silva PE. Inhaled corticosteroids increase the risk of oropharyngeal colonization by Streptococcus pneumoniae in children with asthma. *Respirology* 2013; **18**: 272-277 [PMID: 23039314 DOI: 10.1111/j.1440-1843.2012.02280.x]
41 **Nicoletti C**, Brandileone MC, Guerra ML, Levin AS. Prevalence, serotypes, and risk factors for pneumococcal carriage among HIV-infected adults. *Diagn Microbiol Infect Dis* 2007; **57**: 259-265 [PMID: 17292578 DOI: 10.1016/j.diagmicrobio.2006.08.021]
42 **Onwubiko C**, Swiatlo E, McDaniel LS. Cross-sectional study of nasopharyngeal carriage of Streptococcus pneumoniae in human immunodeficiency virus-infected adults in the conjugate vaccine era. *J Clin Microbiol* 2008; **46**: 3621-3625 [PMID: 18845823 DOI: 10.1128/JCM.01245-08]
43 **Weinberger DM**, Harboe ZB, Viboud C, Krause TG, Miller M, Mølbak K, Konradsen HB. Pneumococcal disease seasonality: incidence, severity and the role of influenza activity. *Eur Respir J* 2014; **43**: 833-841 [PMID: 24036243 DOI: 10.1183/09031936.00056813]
44 **Weinberger DM**, Harboe ZB, Viboud C, Krause TG, Miller M, Mølbak K, Konradsen HB. Serotype-specific effect of influenza on adult invasive pneumococcal pneumonia. *J Infect Dis* 2013; **208**: 1274-1280 [PMID: 23901093 DOI: 10.1093/infdis/jit375]
45 **Microbiologic Information System, National Epidemiology Center, Institute of Health Carlos III.** Annual Report (2012) of Microbiologic Information System. Spain: Madrid, 2014
46 **Hausdorff WP**, Bryant J, Paradiso PR, Siber GR. Which pneumococcal serogroups cause the most invasive disease: implications for conjugate vaccine formulation and use, part I. *Clin Infect Dis* 2000; **30**: 100-121 [PMID: 10619740 DOI: 10.1086/313608]
47 **Belvisi V**, Del Borgo C, Morelli F, Marocco R, Tieghi T, Fabietti P, Vetica A, Lichtner M, Mastroianni CM. Late onset invasive pneumococcal disease in a liver transplanted patient: beyond the Austrian syndrome. *Transpl Infect Dis* 2013; **15**: E111-E114 [PMID: 23581282 DOI: 10.1111/tid.12083]
48 **Imhof A**, Maggiorini M, Zbinden R, Walter RB. Fatal necrotizing fasciitis due to Streptococcus pneumoniae after renal transplantation. *Nephrol Dial Transplant* 2003; **18**: 195-197 [PMID: 12480983 DOI: 10.1093/ndt/18.1.195]
49 **Yu VL**, Chiou CC, Feldman C, Ortqvist A, Rello J, Morris AJ, Baddour LM, Luna CM, Snydman DR, Ip M, Ko WC, Chedid MB, Andremont A, Klugman KP. An international prospective study of pneumococcal bacteremia: correlation with in vitro resistance, antibiotics administered, and clinical outcome. *Clin Infect Dis* 2003; **37**: 230-237 [PMID: 12856216 DOI: 10.1086/377534]
50 **Kalin M**, Ortqvist A, Almela M, Aufwerber E, Dwyer R, Henriques B, Jorup C, Julander I, Marrie TJ, Mufson MA, Riquelme R, Thalme A, Torres A, Woodhead MA. Prospective study of prognostic factors in community-acquired bacteremic pneumococcal disease in 5 countries. *J Infect Dis* 2000; **182**: 840-847 [PMID: 10950779 DOI: 10.1086/315760]
51 **Dupont PJ**, Manuel O, Pascual M. Infection and chronic allograft dysfunction. *Kidney Int Suppl* 2010; **119:** S47-S53 [PMID: 21116318 DOI: 10.1038/ki.2010.423]
52 **Centers for Disease Control and Prevention.** Immunization of Health-Care Workers: Recommendations of the Advisory Committee on Immunization Practices (ACIP) and the Hospital Infection Control Practices Advisory Committee (HICPAC). *MMWR Recommendations and Reports* 1997; **46**: 1-24
53 **Advisory Committee on Immunization Practices.** Preventing pneumococcal disease among infants and young children. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recommendations and Reports* 2000; **49:** 1-35
54 **Moberley S**, Holden J, Tatham DP, Andrews RM. Vaccines for preventing pneumococcal infection in adults. *Cochrane Database Syst Rev* 2013; **1**: CD000422 [PMID: 23440780 DOI: 10.1002/14651858.CD000422.pub3]
55 **Shapiro ED**, Berg AT, Austrian R, Schroeder D, Parcells V, Margolis A, Adair RK, Clemens JD. The protective efficacy of polyvalent pneumococcal polysaccharide vaccine. *N Engl J Med* 1991; **325**: 1453-1460 [PMID: 1944423 DOI: 10.1056/NEJM199111213252101]
56 **Jackson LA**, Neuzil KM, Yu O, Benson P, Barlow WE, Adams AL, Hanson CA, Mahoney LD, Shay DK, Thompson WW. Effectiveness of pneumococcal polysaccharide vaccine in older adults. *N Engl J Med* 2003; **348**: 1747-1755 [PMID: 12724480 DOI: 10.1056/NEJMoa022678]
57 **Musher DM**, Rueda-Jaimes AM, Graviss EA, Rodriguez-Barradas MC. Effect of pneumococcal vaccination: a comparison of vaccination rates in patients with bacteremic and nonbacteremic pneumococcal pneumonia. *Clin Infect Dis* 2006; **43**: 1004-1008 [PMID: 16983612 DOI: 10.1086/507699]
58 **Huss A**, Scott P, Stuck AE, Trotter C, Egger M. Efficacy of pneumococcal vaccination in adults: a meta-analysis. *CMAJ* 2009; **180**: 48-58 [PMID: 19124790 DOI: 10.1503/cmaj.080734]
59 **Silberman H**, Overturf GD, Field RJ, Butler J, Berne TV, Witt R. Pneumococcal vaccination in recipients of renal allografts. *Surg Forum* 1979; **30**: 156-157 [PMID: 44020]
60 **Marrie TJ**, Schiffman G, Bortolussi R, Field C, Whalen A. Humoral immune response of kidney transplant recipients to pneumococcal vaccine. *Proc Soc Exp Biol Med* 1981; **167**: 62-69 [PMID: 7015353]
61 **Cosio FG**, Giebink GS, Le CT, Schiffman G. Pneumococcal vaccination in patients with chronic renal disease and renal allograft recipients. *Kidney Int* 1981; **20**: 254-258 [PMID: 6169871 DOI: 10.1038/ki.1981.128]
62 **Linnemann CC**, First MR, Schiffman G. Response to pneumococcal vaccine in renal transplant and hemodialysis patients. *Arch Intern Med* 1981; **141**: 1637-1640 [PMID: 7030249 DOI: 10.1001/archinte.1981.00340130081018]
63 **Linnemann CC**, First MR, Schiffman G. Revaccination of renal transplant and hemodialysis recipients with pneumococcal vaccine. *Arch Intern Med* 1986; **146**: 1554-1556 [PMID: 3524494 DOI: 10.1001/archinte.1986.00360200116019]
64 **Arnold WC**, Steele RW, Rastogi SP, Flanigan WJ. Response to pneumococcal vaccine in renal allograft recipients. *Am J Nephrol* 1985; **5**: 30-34 [PMID: 3881958 DOI: 10.1159/000166899]
65 **Rytel MW**, Dailey MP, Schiffman G, Hoffmann RG, Piering WF. Pneumococcal vaccine immunization of patients with renal impairment. *Proc Soc Exp Biol Med* 1986; **182**: 468-473 [PMID: 3526355]
66 **Dengler TJ**, Strnad N, Bühring I, Zimmermann R, Girgsdies O, Kubler WE, Zielen S. Differential immune response to influenza and pneumococcal vaccination in immunosuppressed patients after heart transplantation. *Transplantation* 1998; **66**: 1340-1347 [PMID: 9846520 DOI: 10.1097/00007890-199811270-00014]
67 **Blumberg EA**, Brozena SC, Stutman P, Wood D, Phan HM,

Musher DM. Immunogenicity of pneumococcal vaccine in heart transplant recipients. *Clin Infect Dis* 2001; **32**: 307-310 [PMID: 11170924 DOI: 10.1086/318482]

68 **McCashland TM**, Preheim LC, Gentry MJ. Pneumococcal vaccine response in cirrhosis and liver transplantation. *J Infect Dis* 2000; **181**: 757-760 [PMID: 10669371 DOI: 10.1086/315245]

69 **Kazancioğlu R**, Sever MS, Yüksel-Onel D, Eraksoy H, Yildiz A, Celik AV, Kayacan SM, Badur S. Immunization of renal transplant recipients with pneumococcal polysaccharide vaccine. *Clin Transplant* 2000; **14**: 61-65 [PMID: 10693637 DOI: 10.1034/j.1399-0012.2000.140111.x]

70 **Pourfarziani V**, Ramezani MB, Taheri S, Izadi M, Einollahi B. Immunogenicity of pneumococcal vaccination in renal transplant recipients and hemodialysis patients: a comparative controlled trial. *Ann Transplant* 2008; **13**: 43-47 [PMID: 18806734]

71 **Centers for Disease Control and Prevention.** Licensure of 13-Valent Pneumococcal Conjugate Vaccine for Adults Aged 50 Years and Older. Available from: URL: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6121a3.htm

72 **Food and Drug Administration.** FDA expands use of Prevnar 13 vaccine for people ages 50 and older. Silver Spring (MD): US Department of Health and Human Services. USA: Food and Drug Administration, 2011: 26-40

73 **Danziger-Isakov L**, Kumar D. Vaccination in solid organ transplantation. *Am J Transplant* 2013; **13** Suppl 4: 311-317 [PMID: 23465023 DOI: 10.1111/ajt.12122]

74 **Food and Drug Administration.** Vaccines and Related Biological Products Advisory Committee (VRBPAC) adult indication briefing document: Prevnar 13. Silver Spring, MD: US Department of Health and Human Services. USA: Food and Drug Administration, 2011

75 **Chen J**, O'Brien MA, Yang HK, Grabenstein JD, Dasbach EJ. Cost-effectiveness of pneumococcal vaccines for adults in the United States. *Adv Ther* 2014; **31**: 392-409 [PMID: 24718851 DOI: 10.1007/s12325-014-0115-y]

76 **Cordero E**, Aydillo TA, Perez-Ordoñez A, Torre-Cisneros J, Lara R, Segura C, Gentil MA, Gomez-Bravo MA, Lage E, Pachon J, Perez-Romero P. Deficient long-term response to pandemic vaccine results in an insufficient antibody response to seasonal influenza vaccination in solid organ transplant recipients. *Transplantation* 2012; **93**: 847-854 [PMID: 22377789 DOI: 10.1097/TP.0b013e318247a6ef]

77 **Mufson MA**, Krause HE, Schiffman G. Reactivity and antibody responses of volunteers given two or three doses of pneumococcal vaccine. *Proc Soc Exp Biol Med* 1984; **177**: 220-225 [PMID: 6483857 DOI: 10.3181/00379727-177-41934]

78 **Kumar D**, Rotstein C, Miyata G, Arlen D, Humar A. Randomized, double-blind, controlled trial of pneumococcal vaccination in renal transplant recipients. *J Infect Dis* 2003; **187**: 1639-1645 [PMID: 12721944 DOI: 10.1086/374784]

79 **Kumar D**, Welsh B, Siegal D, Chen MH, Humar A. Immunogenicity of pneumococcal vaccine in renal transplant recipients--three year follow-up of a randomized trial. *Am J Transplant* 2007; **7**: 633-638 [PMID: 17217436 DOI: 10.1111/j.1600-6143.2007.01668.x]

80 **Kumar D**, Chen MH, Wong G, Cobos I, Welsh B, Siegal D, Humar A. A randomized, double-blind, placebo-controlled trial to evaluate the prime-boost strategy for pneumococcal vaccination in adult liver transplant recipients. *Clin Infect Dis* 2008; **47**: 885-892 [PMID: 18715160 DOI: 10.1086/591537]

81 **Tobudic S**, Plunger V, Sunder-Plassmann G, Riegersperger M, Burgmann H. Randomized, single blind, controlled trial to evaluate the prime-boost strategy for pneumococcal vaccination in renal transplant recipients. *PLoS One* 2012; **7**: e46133 [PMID: 23029408 DOI: 10.1371/journal.pone.0046133]

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CASE REPORT

Non chylous filarial ascites: A rare case report

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Author contributions: Shah KS and Bhate PA designed the case and wrote the paper; Solanke D and Pandey V collected clinical data; case report was guided by Ingle MA and Sawant P; cytological examination was performed by Kane SV.
Ethics approval: The ethics committee functions as per ICH-GCO, schedule Y guidelines.
Informed consent: The patient is not revealed.
Conflict-of-interest: All the authors of thia case report state that there is no conflict of interest involved.

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Abstract

Filariasis is a common health problem in tropical and subtropical regions including India. It commonly presents with lymphatic involvement in form of nonpitting pedal edema, chylous ascites, chyluria, hydrocele and lymphocele. Detection of microfilaria in ascitic fluid is an extremely uncommon finding. We present a case of non chylous ascites where microfilaria were detected in the ascitic fluid.

Key words: Microfilaria; Postpartum ascites; Non chylous ascites

Core tip: We report a rare case of postpartum ascites caused by filarial infection. There are only a few case reports where microfilaria were detected in ascitic fluid; among these, non chylous ascitis is even rarer.

Shah KS, Bhate PA, Solanke D, Pandey V, Ingle MA, Kane SV, Sawant P. Non chylous filarial ascites: A rare case report. *World J Clin Infect Dis* 2015; 5(1): 11-13 Available from: URL: http://www.wjgnet.com/2220-3176/full/v5/i1/11.htm DOI: http://dx.doi.org/10.5495/wjcid.v5.i1.11

INTRODUCTION

Filarial infection is common in various Asian and African countries. It presents with various manifestations like ascites, pleural effusion and pedal edema; it may even be asymptomatic. We present an interesting and rare case of filariasis in ascitic fluid in postpartum female.

CASE REPORT

A 26 years old female residing in Uttar Pradesh, India, who was 2 mo postpartum, presented with chief complaints of abdominal pain and vomiting since 1 mo and abdominal distention since 15 d. The pain was in periumbilical, non radiating, dull, mild and continuous. It was associated with non-

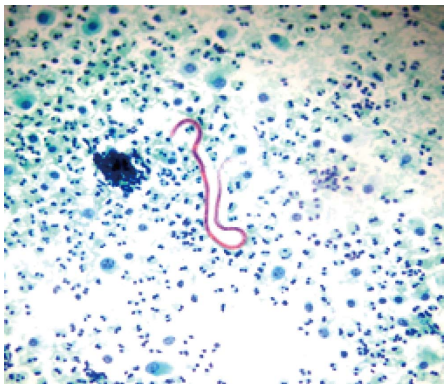

Figure 1 Ascitic fluid-Smear shows Microfilaria. Background shows inflammatory cells (Pap stain 100 ×).

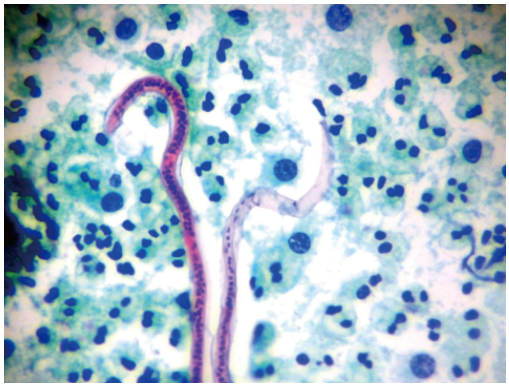

Figure 2 Microfilaria with nuclei. Note that the tail portion is devoid of the nuclei (pap 400 ×).

bilious vomiting, 2-3 episodes per day. She also complained of abdominal distention from the last 15 d, which was generalized and gradually increasing with increasing abdominal pain. She had undergone a Caesarean section 2 mo ago. The pregnancy had been uneventful. Her general physical, cardiovascular and respiratory systems examination did not reveal any abnormalities. Shifting dullness was present on abdominal examination without tenderness or hepatosplenomegaly.

Laboratory examination revealed haemoglobin of 12.2 gm%, normal mean corpuscular volume (MCV) of 82fl, total leukocyte count of 16500/cmm and platelet count of 253000/cmm. Creatinine was 1.2 mg%, AST (aspartate aminotransferase) 21 IU/L, ALT (alanine aminotransferase) 25 IU/L and Bilirubin 1.1 mg/dL. Her total serum protein was 6.4 g/dL, albumin 3.7 g/dL and INR (international normalised ratio) 1.1, serum cholesterol and TG (triglycerides) were normal. Serum amylase was 45 IU/L and serum LDH (lactate dehydrogenase) was 1241 IU/L. Stool examination was normal. Ascitic fluid analysis revealed straw coloured fluid, total leukocyte count of 876 cells/mm^3 with 65% neutrophils, ascitic protein 3.7 g/dL, ascitic albumin of 2.7 g/dL and SAAG was 1. Ascitic fluid ADA (adenosine deaminase) was 14 U/L, amylase 46 IU/L, LDH 106 IU/L, glucose 40 mg/dL and TG was 55 mg/dL. Ultrasonography of abdomen was unremarkable except for moderate ascites. Portosplenic Doppler was also normal. CT abdomen was suggestive of moderate ascites, omental and mesenteric fat stranding with multiple non necrotic mesenteric lymph nodes and diffuse long segment concentric wall thickening involving small bowel loops, especially the jejunum. Upper GI endoscopy was normal. She was given IV antibiotics and IV fluids. She improved symptomatically but abdominal distention persisted. Ascitic fluid cytology showed numerous eosinophils, few neutrophils, mesothelial cells and few histiocytes. Cytology was negative for malignant cells. But cytological examination revealed presence of sheathed microfilariae consistent with Wuchereria Bancrofti (Figures 1 and 2). Subsequently patient's peripheral smear examination showed presence of motile microfilaria which confirmed our diagnosis (Figure 3). She was given diethylcarbamazine 300 mg/d for 21 d along with albendazole 400 mg/d for 7 d. She responded well to treatment; abdominal pain and ascites disappeared in a few days. Peripheral blood smear repeated after two weeks was negative for microfilaria.

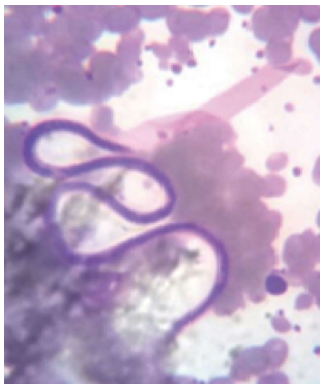

Figure 3 Microfilaria in peripheral smear. Sample collected at 2 am.

DISCUSSION

We report a case of non chylous filarial ascites positive for microfilaria in ascitic fluid which is a rare finding. To the best of our knowledge, there are only two published cases where microfilaria were detected in ascitic fluid[1,2].

Filariasis is still endemic in many parts of world including India and a predominant cause of health morbidity. It is quite prevalent in many states of India like Jharkhand, Andhra Pradesh, Uttar Pradesh, Gujarat, Orissa, Tamil Nadu, Kerala and Bihar. Many infected patients remain asymptomatic.

The definitive host for filarial infection is man. The parasites have a predilection for lymphatics. The Culex mosquito is an intermediate vector. They ingest microfilariae from affected individuals and

this larvae develop into active motile forms in 10-12 d for further transmission into a new host. In the definitive host, the larvae develop into adult worms in lymphatics and give rise up to 50000 worms/d.

The adult worm usually resides in lymphatics while microfilariae traverse in peripheral blood. Microfilaria are visible in specimens of tissue or fluids due to obstruction of lymphatics and vascular channels. Inflammatory conditions, major trauma, even stasis or tumours can precipitate obstruction. Due to this obstruction, there is lymphatic damage and extravasation of microfilariae. Based on the detection of microfilariae in blood samples and body fluids, we establish our diagnosis. On autopsy, adult filarial parasites can be demonstrated.

Moreover, pregnancy is associated with pelvic congestion due to effect of progesterone and other placental hormones. Hypothetically, caesarean section could be a cause of traumatic rupture of lymphatic vessel with subsequent spread of microfilariae into the peritoneal cavity[3].

Ascites and pleural effusion are uncommon findings. Commonly they are chylous in nature due to blockage of lymph from the occluded lymphatic channels. Such microfilarial ascites being non-chylous microfilarial ascites is extremely rare. Lymphangitis because of partial obstruction is a proposed mechanism for such exudative collection[4]. Ascitic fluid TG could also be low due to inadequate diet, but ascitic fluid TG content is low in our patient inspite of adequate food intake.

Many authors have reported microfilariae in breast lump as well as in lymph node aspirates[5,6]. Microfilariae have been detected in thyroid swelling and rarely in subcutaneous swellings[7,8]. Detection of microfilaria in body fluids like pleural effusion and ascites is rare and such ascites being non chylous is extremely rare.

Therefore clinical suspicion and careful cytological examination is extremely important to avoid misdiagnosis. Demonstration of parasite in cytology will be helpful not only in the right diagnosis but also in instituting specific treatment.

COMMENTS

Case characteristics

Vomiting since 1 mo and abdominal distention since 15 d.

Clinical diagnosis

Ascites on percussion of abdomen without organomegaly.

Differential diagnosis

Twenty six years old female 2 mo postpartum presented with complaints of abdominal pain and Vomiting since 1 mo and abdominal distention since 15 d. Budd chiari syndrome, decompensated chronic liver disease, tuberculosis.

Laboratory diagnosis

Normal CBC, liver function and metabolic panel except high leukocyte count with ascitic fluid showing high leukocytes with low protein and normal ADA level.

Imaging diagnosis

CT abdomen was done which was suggestive of moderate ascites, omental and mesenteric fat stranding with multiple non necrotic mesenteric lymph nodes and diffuse long segment concentric wall thickening involving small bowel loops especially jejunum with normal ultrasound and colour Doppler study.

Pathological diagnosis

Ascitic cytology revealed presence of numerous neutrophils with presence of microfilaria of W Bancrofti.

Treatment

Patient was treated with diethylcarbamazine for 21 d and albendazole for 7 d.

Related reports

Presence of microfilaria has been documented in atypical location by FNA has been documented by Yenkeshwar PN and others but detection of microfilaria in ascitic fluid is very uncommon.

Experiences and lessons

Clinical suspicion and careful cytological examination by expert pathologist is extremely important in clinical practice.

Peer review

Shah and colleagues present an interesting and very rare case of ascites due to filariasis in a young woman a few weeks after giving birth.

REFERENCES

1 **Yenkeshwar PN**, Kumbhalkar DT, Bobhate SK. Microfilariae in fine needle aspirates: a report of 22 cases. *Indian J Pathol Microbiol* 2006; **49**: 365-369 [PMID: 17001886]

2 **Mitra SK**, Mishra RK, Verma P. Cytological diagnosis of microfilariae in filariasis endemic areas of eastern Uttar Pradesh. *J Cytol* 2009; **26**: 11-14 [PMID: 21938142 DOI: 10.4103/0970-9371.51333]

3 **Babic I**, Tulbah M, Ghourab S. Spontaneous resolution of chylous ascites following delivery: a case report. *J Med Case Rep* 2012; **6**: 187 [PMID: 22762446 DOI: 10.1186/1752-1947-6-187]

4 **Walter A**, Krishnaswami H, Cariappa A. Microfilariae of Wuchereria bancrofti in cytologic smears. *Acta Cytol* 1983; **27**: 432-436 [PMID: 6349200]

5 **Varghese R**, Raghuveer CV, Pai MR, Bansal R. Microfilariae in cytologic smears: a report of six cases. *Acta Cytol* 1996; **40**: 299-301 [PMID: 8629415]

6 **Pandit AA**, Shah RK, Shenoy SG. Adult filarial worm in a fine needle aspirate of a soft tissue swelling. *Acta Cytol* 1997; **41**: 944-946 [PMID: 9167733]

7 **Joshi AM**, Pangarkar MA, Ballal MM. Adult female Wuchereria bancrofti nematode in a fine needle aspirate of the lymph node. *Acta Cytol* 1995; **39**: 138 [PMID: 7847003]

8 **Dey P**, Walker R. Microfilariae in a fine needle aspirate from a skin nodule. *Acta Cytol* 1994; **38**: 114 [PMID: 8291349]

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