International travel in the immunocompromised patient: a cross-sectional survey of travel advice in 254 consecutive patients

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Abstract

Aims: Our primary aim was to determine the rate of overseas travel in immunocompromised individuals attending appropriate clinics at an Australian tertiary care hospital. We also aimed to characterise health-seeking behaviour prior to travel and investigated sources of pre-travel advice, compared travel patterns and activities between three specific immunosuppressed groups, and examined pre-immunosuppression patient serology.

Methods: We implemented a cross-sectional survey of patients between February and August 2012. This survey was implemented among three outpatient populations at Monash Medical Centre, an Australian tertiary care hospital.

Results: We recruited 254 immunosuppressed adults from three patient populations: human immunodeficiency virus-positive individuals, renal transplant patients and rheumatology patients requiring immunosuppressive therapy. No clinical intervention was performed. In the 10 years preceding the survey, 153 (60.2%) participants reported international travel. Of these, 105 (68.6%) were immunosuppressed at the time of travel. These patients were 47.6% male and 60% Australian born. Forty per cent were visiting friends and relatives as part of their travel. Fifty-four per cent of those immunocompromised at the time of travel were going to high-risk destinations. Pathology files indicated that serological screening was frequently not performed prior to immunosuppression in the renal transplant and rheumatology groups.

Conclusions: Immunocompromised patients often travel to high-risk destinations with limited or inadequate pre-travel preparations. Doctors caring for the immunocompromised should be aware of travel risks, suitable vaccination protocols and when to refer to specialist travel clinics.

Introduction

There are currently more than 900 million international journeys undertaken each year,1 with international travel estimated to increase to approximately 1.6 billion travellers by 2020, with the largest increase to tropical and subtropical areas.2

Reported rates of travel-related illnesses range from 30% to 60% of international travellers;3–5 however, reports suggest that as few as 8% of all those travelling seek pre-travel advice from a medical practitioner.6 The pre-travel consultation is the main method of educating and advising travellers about strategies to reduce the rates of travel-related illness.

Pre-travel advice is especially recommended for immunocompromised travellers as they may be at an increased risk of exotic, rare or opportunistic infections,7,8 as well as suffering from more severe and protracted disease9 compared with immunocompetent hosts. Vaccination may be problematic as live vaccines (measles, Bacille Calmette–Guérin, yellow fever, varicella zoster virus, and live Japanese encephalitis and oral typhoid vaccines) are contraindicated10 and inactivated vaccines may produce suboptimal immune responses. Drug interactions between travel medicine drugs and immunosuppressive mediation or human
immunodeficiency virus (HIV) drug regimens may also occur, highlighting the need to provide expert advice to some of these patients. Furthermore, although many immunocompromised travellers are aware of their increased infectious disease risk, studies indicate that they are equally likely to engage in risk behaviours as healthy travellers.11

Given these risks for immunocompromised travellers, it is important to understand the determinants of health-seeking behaviour and medical advice, as well as the travel patterns and behaviours in these patient populations to ensure these travellers are receiving adequate advice for disease prevention.

Methods

A cross-sectional survey to compare international travel patterns and travel health practice in three populations of immunocompromised patients was undertaken at a 640-bed tertiary referral hospital in Melbourne, Australia. Project approval was obtained from the Monash Health Human Research Ethics Committee.

Survey participants were recruited from three outpatient populations: HIV-positive individuals, renal transplant patients and rheumatology patients requiring immunosuppressive therapy. The participants were asked to complete a questionnaire that included demographic, previous immunisation history, previous travel history (within the past ten years) and, for the most recent trip, pre-travel advice, vaccinations, chemoprophylaxis, risk-taking behaviours and travel-related illness (Appendix SI).

Hospital pathology results, including serological testing for infections that are common in our population and can reactivate with immunosuppression or require a live vaccine, were collected. Serology results for hepatitis A and B viruses (HAV & HBV), measles and varicella were assessed.

Definitions

For the purposes of a comparative analysis, travel destinations were designated ‘high-risk’ or ‘low-risk’. A destination was considered high-risk if vaccinations against HAV and typhoid were recommended in the vaccination guidelines from the Centres for Disease Control.12 The Australian Immunisation Handbook recommends a booster typhoid vaccination every 3 years for travellers using the more commonly supplied vaccines and every 5 years for four doses of the oral vaccine, though the latter is generally not given to immunocompromised travellers.13 Individuals travelling to a high-risk country, as defined in this study, might reasonably be expected to see a doctor for this vaccination prior to travel.

The SPSS software package was used to analyse data from the questionnaires. Categorical variables were analysed using the Pearson’s Chi-Squared test or the Fisher’s exact test (where values were less than five). For scale data, analysis of variance was used to compare results from the three groups of immunosuppressed patients. Comparisons were performed between participant groups, with \( P \) values <0.05 considered statistically significant. Missing values were excluded from calculations of percentages and from statistical analyses.

Results

Demographic data

The questionnaire was completed by 256 individuals: 56 HIV-infected individuals, 100 renal transplant patients and 100 rheumatology patients. Two patients were excluded because their only travel history was immigration to Australia. Data from 254 participants were included in the analysis.

Of our immunocompromised participants, 153 (60.2%) reported international travel in the 10 years preceding the survey; 105 (68.6%) reported themselves as having been immunosuppressed at the time of travel. This subgroup was the focus of our analysis (Table 1).

Overall, the mean age of those who were immunocompromised at the time of travel was 53.1 years and 47.6% were male. Forty per cent of travellers had completed a tertiary education and 91.4% reported English as their first language.

Rates of international travel

Of the 105 participants who were immunosuppressed during their travel, the median number of overseas trips was 3.00 (range 1 to 30) during the survey period. Fifty-seven (54.3%) reported travel to at least one high-risk destination. Of those who travelled to visit friends and relatives, 63.4% went to a high-risk destination compared with 48.4% in those who travelled for other reasons (\( P = 0.13 \)).

Sources of pre-travel advice and activities that increase risk of infection

Regarding their most recent trip, 72/105 (68.6%) immunocompromised travellers sought pre-travel advice,
most frequently from their treating specialist or general practitioner (GP). Travel clinics were used in 4/105 (3.8%) of patients. Participants were more likely to seek advice if travelling to a high-risk country (77.2% vs 58.3% P = 0.04). However, only 47.4% of travellers to a high-risk destination reported receiving a vaccination. Of course, the rate of vaccination is an incomplete measure of either the completeness or success of travel advice. Better measures could include rates of behavioural change as well as measures of correlates of protection from vaccination, but these were beyond the scope of this study.

Sixty-nine (65.7%) of 105 immunocompromised travellers reported engaging in risk behaviours that may place them at an increased infectious disease risk. These included 40 travellers eating food from unreliable sources, and 3 reported engaging in sexual activity (only one with a condom).

Of the immunosuppressed patients, 32.4% reported being unwell while travelling; however, of these, only half (17.1%) sought medical advice. Eight immunosuppressed patients (7.9%) ran out of their usual medications.

### Serological testing

Results of HAV, HBV, measles and varicella virus serology are described in Table 2. A large proportion of patients did not have serological tests done to examine their immune status for these vaccine preventable diseases. Only 7.9% and 4.3% were tested for varicella and measles respectively, 59.3% had testing for HBV immunity, and 18.7% for HAV immunity.

Testing for varicella and measles was limited in all sampled patient populations. HAV testing was more likely in the HIV population, and rheumatology patients were less likely to have HBV testing than the other groups.

### Discussion

Our study investigated the rates and patterns of international travel, and travel health practices in immunocompromised individuals. The most important findings of our study were that Australian immunocompromised patients frequently travel internationally, including to high-risk destinations (54.3%) and may not seek...
pre-travel advice and prophylaxis despite participating in potentially risky behaviour. Two thirds of participants sought pre-travel advice, usually from their particular specialist (e.g. transplant physician or rheumatologist) or GP. Of the patients who did seek advice, reported vaccination levels were low, and pre-travel screening appears to be inadequate.

Rates and types of travel

Immunocompromised patients have high rates of international travel, and frequently travel to high-risk destinations. The highest rate of international travel while immunocompromised was seen in rheumatology patients with 44.0%, compared with 42.0% of renal transplant patients, and 35.2% of HIV-positive participants. Our findings are consistent with rates of travel among immunocompromised patient groups reported elsewhere. Studies of HIV-positive individuals estimate that 10–45% travel following their diagnosis. Studies of solid organ transplant patients (not specifically renal transplant patients) report the rate of post-transplant travel to be up to 36%. There are limited data available regarding international travel in rheumatology patients. Despite the infectious disease risks, travel to a high-risk destination is often part of the itinerary of the immunocompromised traveller. Of participants who were immunosuppressed at the time of travel, 54.3% reported travelling to a high risk destination. This is important because travel-related illnesses are known to have a longer clinical course of infection, with increased severity and a higher rate of complications.

HIV-infected patients with a low CD4+ count (<200 cells/mm3) are at increased risk of infection and complications when travelling to resource-poor settings. In our population, four HIV-positive individuals had a low CD4+ count at the time of travel, three of these individuals travelled to a high-risk destination, placing them at some increased risk of infection.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Serology results for 241 immunosuppressed patients (13 patients had no pathology testing done at our service)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HIV positive</td>
</tr>
<tr>
<td>n = 54</td>
<td>n = 96</td>
</tr>
<tr>
<td>Varicella zoster virus</td>
<td>IgG positive</td>
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<tr>
<td></td>
<td>IgG negative</td>
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<tr>
<td></td>
<td>Test not done</td>
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<tr>
<td>Measles virus</td>
<td>IgG positive</td>
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<tr>
<td></td>
<td>IgG negative</td>
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<tr>
<td></td>
<td>Test not done</td>
</tr>
<tr>
<td>Hepatitis B virus</td>
<td>HBSAb positive or HbcAb positive</td>
</tr>
<tr>
<td></td>
<td>HbsAb and HbcAb negative</td>
</tr>
<tr>
<td></td>
<td>Previously HbsAb positive but not detected on last test</td>
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<tr>
<td></td>
<td>HbsAb test not done</td>
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<tr>
<td>Hepatitis A virus</td>
<td>IgG positive</td>
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<td></td>
<td>IgG negative</td>
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<td></td>
<td>Test not done</td>
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</tbody>
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**HBcAb, Hepatitis B core antibody; HbsAb, Hepatitis B surface antibody.**

Immunocompromised individuals have low rates of pre-travel advice

In general, there was a low reported rate of seeking pre-travel advice in the study population regardless of education level and contrary to the general medical literature, which identifies a direct relationship between low levels of education and low rates of health-seeking behaviour. Another unexpected finding was the participants of a non-English-speaking background (NESB) were more likely to seek pre-travel advice; due to the small sampling size of this population, such a finding may be a sampling error or it may indicate a better informed assessment of the risks of travel.

Individuals who travel for the purpose of visiting friends and relatives (VFR) are generally considered to be a high-risk group for contracting infections. This is due to well-documented issues involving low rates of pre-travel advice, poor adherence to travel advice and higher rates of travel to underdeveloped countries. Contrary to expectations, VFR travellers in our study were more likely to seek pre-travel health advice, and did not report higher rates of travel to high-risk destinations, or illness during travel.
Immunocompromised travellers are not attending travel clinics for advice

Of immunocompromised travellers, 68.6% sought pre-travel advice. Of these, HIV-positive travellers and renal transplant travellers most commonly consulted their specialists, while travellers in the rheumatology group most commonly sought advice from a GP. This identifies a potential intervention for the improvement of patient care: specialists and GPs are common sources for travel advice, as such, identifying gaps in knowledge and educating these groups about travel and risks may reduce the risk of travel-related illness for the immunosuppressed patient.

A small minority (10.4%) of participants sought advice from a travel medicine clinic that provides highly specialised pre-travel medical advice. Travel clinics in Australia have been found to provide superior advice to GPs, however, patients most in need of this service are often not referred.

A majority of travellers who did not seek pre-travel advice travelled to a high-risk destination, and many reported that they did not believe they required pre-travel advice, indicating a need for patient education regarding the risks of travelling with a compromised immune system.

Doctors may not be ordering serological testing prior to immunosuppression

Serological screening and appropriate vaccination prior to immunosuppression are widely recommended, both for solid organ transplant patients and for patients requiring other immunosuppressive therapy. These are particularly important in conditions that may reactivate or that require a live vaccine so cannot be administered after the patient is immunosuppressed.

Measles and varicella are common childhood diseases that occur in adults, and are preventable by live vaccination. However, live vaccination is contraindicated for individuals with severely impaired immune function due to the increased risk of disseminated disease; therefore, screening, and vaccination if required, should occur prior to starting an immunosuppressive regimen. Serological screening for measles is of particular concern for those vaccinated as children between 1968 and 1984 in Australia, as these individuals may have received inadequate vaccination. In our study, 96.7% were not tested for measles, and 92.1% were not tested for varicella. Guidelines recommend moving to universal HBV vaccination, and HAV vaccination for travellers to risk areas. Despite this, 40.7% of our immunosuppressed travellers were not tested for HBV. The significance of these data is limited because it only examines pathology testing done at our service, and did not include risk of exposure of history or of disease as part of the analysis. However, the results suggest that more could be done to check immunity, and where required and possible, vaccination of these patients prior to immunosuppression could be helpful in preventing future complications.

Doctors may not be performing adequate patient education

In this immunosuppressed population, 38.1% of travellers reported engaging in risk behaviours during their trip. Other studies have also found that immunosuppressed travellers are equally likely to engage in risk behaviours as healthy travellers. In our study, surveyed risk-taking behaviours were reported more frequently in the HIV-positive travellers. This identifies a potential target group for educational intervention, though how successful such interventions are may remain an area for further study.

Limitations of the study

There were several limitations encountered during the course of the study period. Importantly, the retrospective nature of the study presents the issue of recall or other similar bias for example with respect to rates of unprotected sex.

In addition, we did not keep records of the number of patients who elected not to complete the survey, limiting our capacity to comment on the nature of any potential selection bias in our results. This study also has fewer patients of NESB and HIV-positive participants than expected, limiting the confidence that these results are representative of the entire patient population.

Conclusions

Immunocompromised patients travel overseas including to high-risk destinations, and this study demonstrates that they may be doing so with inadequate education and vaccination. The study contributes to the body of literature on this topic, particularly the inclusion of the rheumatological group as there is little information regarding travel patterns in this population.

Future directions

The data from our study highlight several issues relating to the care of the immunocompromised patient, particularly the high proportion of travel to high-risk
destinations with limited travel-related education and vaccination. Further studies would have to be undertaken to determine what educational and vaccination-related interventions might lead to decreased infection rates in immunosuppressed travellers, but of necessity these studies would in part need to be much larger.

Doctors caring for the immunocompromised should be aware of travel risks, suitable vaccination protocols and when to refer to specialist travel clinics.

References