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Post stem cell transplantation revaccination: A survey of the current practices in India

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ABSTRACT

Background: Hematopoietic stem cell transplant (HSCT) recipients are more susceptible to infections from vaccine preventable diseases (VPDs) than the general population. Indian stem cell transplant registry (ISCTR) post-BMT vaccination guidelines were formulated in 2015. The objective of the survey was to assess the compliance to these guidelines among transplant physicians in India.

Materials and methods: This is a cross-sectional survey executed as the quantitative research strategy to explore the various aspects of vaccination practices among transplant physicians in India. The 'data collection tool' included 36 predetermined questions related to vaccination of the patients and their close contacts. Theoretical construct of the questionnaire was face-validated and questionnaire survey forms were emailed individually as attachments or by google forms. This study is being reported based on the checklist for reporting results of internet e-surveys statement guidelines.

Results: Survey forms were sent to 105 transplant physicians in India, 62% of whom responded representing 78.8% of transplant centers in India. More than 90% of allogeneic transplant physicians and 64% of autologous transplant physicians offered vaccination. Over two third of the physicians responded that they would discontinue vaccination at the onset of cGVHD. Fewer than one third physicians offered vaccination against Hepatitis A, Typhoid or Meningococcal infections. Forty two percent of respondents were unaware of the ISCTR post-BMT vaccination protocol. Only 47% of respondents reported complete adherence to any of the protocols they were following. Immune reconstitution to guide vaccination was available only to 13.3 percent of respondents.

Conclusion: There is a need to improve the implementation strategies of vaccination in HSCT recipients to increase the adherence and continuation of it even in the presence of GVHD. There is also a need to extend the vaccination among VPDs especially prevalent in India.

1. Introduction

Hematopoietic stem cell transplantation (HSCT) is the standard of care for many patients with congenital or acquired disorders of the hematopoietic system and haematological malignancies [1]. As per the Worldwide Network of Blood and Marrow Transplantation (WBMT) report from 77 countries, annually, more than 68,000 transplants are done globally of which 53% are autologous and 47% are allogeneic. An increase of 46% was noted in a span of 6 years from 2006 to 2012 [2]. As per the Indian Stem Cell Transplant Registry (ISCTR) data, from a reported 365 transplants in 2006, there has been a significant growth in the number of transplants in the last decade to more than 2000 transplants annually in 2016. Cumulatively, in a span of 32 years from 1983 to 2016, more than 12,000 transplants have been done in India. (ISCTR annual report, unpublished data).

The number of long term survivors have increased over the years as the outcomes of transplantation have improved with the enhanced supportive care and advanced human leukocyte antigen (HLA) typing techniques. However, infections remain a major challenge despite these advances leading to significant morbidity and

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mortality post-HSCT especially in the Indian subcontinent. A vaccine-preventable disease (VPD) is an infectious disease for which an effective preventive vaccine exists [3]. Decline in antibody (Ab) titers to VPDs along with impaired humoral immunity is observed within months and may continue years post-HSCT is the rationale for immunizing transplant patients [4]. Among the VPDs, invasive pneumococcal and influenza infections have been reported to increase the risk of mortality and morbidity among HSCT recipients [5,6]. Although uncommon, *Haemophilus influenza* mediated infections, *Bordetella pertussis* and measles virus are the other documented VPDs in HSCT recipients [7–10].

Many major societies (American Blood and Marrow Transplantation, European Group of Blood and Marrow Transplantation, and Infectious Disease Society of America) have published vaccination guidelines separately or as part of broad practice guidelines for preventing infectious complications among blood and marrow transplantation recipients or other immunocompromised hosts [11–14].

Despite these extensive guidelines there seems to be lack of adherence to the vaccination recommendations and clinical practice among various centers in United Kingdom, Australia, United States and Canada [15–18]. A Survey among the principal investigators of the Pediatric Blood and Marrow Transplant Consortium (PBMTC) on the immunization practice patterns after HSCT and compliance with the 2000 CDC guidelines, showed that less than 20% of the centers reported schedules consistent with the 2000 CDC recommendations for both allogeneic and autologous HSCT recipients and emphasized the need to address the use of pneumococcal conjugate vaccine [19]. A recent national survey of the United Kingdom NHS programme highlighted differences in the delivery of routine vaccine programme across a national health-care system with limited quality assurance [20].

Post-HSCT vaccination recommendations for the ISCTR in the Indian context were drafted in 2015 taking into consideration of all the previously published guidelines and prevalence of infections in India [21]. This study was undertaken to estimate the current compliance rates with vaccination guidelines, assess the knowledge and real world practice patterns among the BMT physicians in India and to determine future strategies for best practices.

2. Materials and methods

This is a 'cross-sectional' survey executed as the quantitative research strategy to explore the various aspects of vaccination practices among transplant physicians in India [22].

The 'data collection tool' [23] was the questionnaire which included 36 predetermined questions related to vaccination to the patients and their close contacts. The questions were closed ended with "yes" "no" responses in 23 and the rest were multiple choice questions. Specific immunization practices for autologous and allogeneic transplants were collected together. Theoretical construct of the questionnaire was face-validated and optimized by pre-testing the questionnaire among 5 experts to identify ambiguous questions, wording and unclear instructions. Response rate was defined as the number of respondents divided by the number of eligible subjects in the sample [24]. This study is being reported based on the CHERRIES (Checklist for Reporting Results of Internet E-Surveys) statement guidelines [25]. The usability and technical functionality of the electronic questionnaire was field tested by a core group before sending them out. The contact mode for the participants was telephone calls and emails to ensure the receipt of the questionnaire. Questionnaires were sent to the bone marrow transplant physicians in India who are part of the ISCTR. Survey forms were emailed individually as attachments or by google forms and responses were captured automatically from 14th February 2017 to 6th March 2017.

This was a voluntary survey where the objectives of the study were described, the duration of 20 min was mentioned, no incentives were offered and an informed consent was taken from each participant prior to the beginning of the survey. All the physicians who took independent decisions on post HSCT vaccination of patients were included in the study. Responses from physicians who did not give consent or those who did not perform HSCT in India were excluded. Data was entered using Microsoft Office Excel. Analysis of data was carried out using SPSS version 21.0. Descriptive statistics was applied for all variables.

3. Results

At total of 105 survey forms were sent and 66 participants (62%) responded. This accounted for 41 of the 52 (78.8%) centers registered with ISCTR in 2016 and covered 12 states and 2 union territories. Two respondents were excluded as they were not making independent decisions about post BMT vaccination. Respondents followed four different types of protocols, namely American Blood and Marrow Transplantation (ABMT) [7.8% (n = 5)], Centre for Disease Control and Prevention (CDC) [12.5% (n = 8)], ISCTR [32.8% (21)], Institutional protocol [40.6%, (n = 26)] and 6.3% (n = 4) did not have any protocol.

Sixty-two respondents managed both allogeneic and autologous transplant patients while 2 respondents treated only autologous transplant patients. Post BMT vaccination was offered by 93.8% (n = 62) allogeneic transplant physicians and 64.1% (n = 41) autologous transplant physicians. Although timing of initiation of vaccination varied among the respondents, 74.2% (n = 46) physicians initiated post allogeneic HSCT vaccinations after 12 months and 63.4% (n = 26) physicians initiated post autologous HSCT vaccinations between 6 and 9 months. (Table 1) All centers practiced initiation of vaccination a between 4 weeks and 6 months after discontinuing the immunosuppressive medications. The practice of

Table 1
Post allogeneic and autologous transplant vaccination details.

	Physicians who performed allogeneic transplants (n = 62) n (%)	Physicians who offered autologous transplants (n = 64) n (%)
Physicians who offered Post-BMT vaccination	60 (93.8)	41 (64.1)
Initiation of post BMT vaccination schedule		
3–6 months	0	5 (12.2)
6–9 months	7 (11.3)	26 (63.4)
9–12 months	5 (8.1)	2 (4.9)
>12 months	46 (74.2)	8 (19.5)
Missing data	2	Nil
Pre-vaccination immunological assessment	8 (13.3)	4 (9.8)

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