Human cord blood-derived viral pathogens as the potential threats to the hematopoietic stem cell transplantation safety: A mini review

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Abstract

Umbilical cord blood (UCB) is a valuable source of hematopoietic stem cells (HSCs) and potential alternative for bone marrow transplantation for patients who lack human leukocyte antigen (HLA)-matched donors. The main practical advantages of UCB over other HSC sources are the immediate availability, lower incidence of graft-versus-host disease, minimal risk to the donor, and lower requirement for HLA compatibility. However, the use of UCB is limited by delayed engraftment and poor immune reconstitution, leading to a high rate of infection-related mortality. Therefore, severe infectious complications, especially due to viral pathogens remain the leading cause of morbidity and mortality during the post-UCB transplantation (UCBT) period. In this context, careful screening and excluding the viral-contaminated UCB units might be an effective policy to reduce the rate of UCBT-related infection and mortality. Taken together, complete prevention of the transmission of donor-derived viral pathogens in stem cell transplantation is not possible. However, having the knowledge of the transmission route and prevalence of viruses will improve the safety of transplantation. To the best of our knowledge, there are few studies that focused on the risk of virus transmission through the UCB transplant compared to other HSC sources. This review summarizes the general aspects concerning the prevalence, characteristics, and risk factors of viral infections with a focus on the impact of viral pathogens on cord blood transplantation safety.

Key words: Cord blood; Transplantation safety; Viral pathogens

Core tip: Severe infectious complications, especially due to viral pathogens remain the leading cause of the post-transplantation morbidity and mortality. In this context, excluding the viral-contaminated umbilical cord blood (UCB) units might be an effective policy to reduce the infection rate after UCB transplantation (UCBT). Complete prevention of the transmission of donor-derived viral pathogens via UCB is not possible. However, having the knowledge of the transmission route and the prevalence of viruses will improve the transplantation safety by controlled patient management. This minireview summarizes the general aspects concerning the prevalence, characteristics and risk factors of viral infections with a focus on the impact on UCBT safety.

INTRODUCTION

In past years, allogeneic hematopoietic stem cell transplantation (allo-HSCT) has made considerable progress in the treatment of a large variety of malignant and nonmalignant disorders. Human leukocyte antigen (HLA)-identical sibling and HLA-matched unrelated donors are typically the first choices, although it can be achieved for only about 30% of patients. So, umbilical cord blood transplantation (UCBT) is an alternative option for patients with no HLA-matched bone marrow donors[1,2].

Benefits of using cord blood cells include immediate availability of banked UCB units, lower incidence of graft-versus-host disease (GVHD), minimal risk to the donor, and a lower requirement for HLA compatibility between the donor and the recipient[3].

Despite these advantages, UCBT is associated with delayed engraftment and poor immune reconstitution, leading to a high rate of infection-related mortality, up to about 50% in several historical series. Viral infections are important causes of morbidity and mortality in patients undergoing allo-HSCT. Therefore, careful screening and testing of UCB units seems be critical to exclude the potential UCB units with viral contaminations and to reduce the risk of UCB-related virus transmission[4,5].

Fortunately, improvements in molecular diagnostic methods, such as Multiplex polymerase chain reaction (PCR) and Real-time quantitative PCR (RQ-PCR) have facilitated the early diagnosis of viral infections and selection of "virus-safe" UCB units[6-8] (Table 1).

There have been significant strides in using UCB stem cells in cellular therapy, particularly those for neurologic[9-11] or hematopoietic[12-14] cell differentiation, because of their excellent therapeutic efficacy in bone marrow recovery and regenerative medicine. However, the necessity of increase of transplantation safety is recommended. To the best of our knowledge, there are few studies that focused on the risk of virus transmission through the UCB transplant compared to other HSC sources.

Here, we reviewed the prevalence, characteristics, and risk factors of viral infections in UCB transplantation settings.

COMMON VIRAL INFECTIONS IN HSCT RECIPIENTS

Cytomegalovirus (CMV)

Human CMV, also known as human herpesvirus-5 (HHV-5), is a ubiquitous beta-herpesvirus that infects 60%-95% of healthy adults worldwide[15]. This virus is the most common cause of congenital infection worldwide, impacting about one million newborns annually[16].

CMV infection is a leading opportunistic infectious agent in allogeneic HSCT. It has been noted that 30% and 5% of the recipients of allogeneic and autologous HSCT develop CMV disease, respectively. Moreover, the risk of CMV transmission from a seropositive donor to a seronegative recipient is about 30%[17,18].

Table 1 Umbilical cord blood transplantation-related viral infection

Virus type	UCBT-related primary viral infection	UCBT-related virus reactivation	Ref.
CMV	Albano *et al*		[4]
	Abedi *et al*		[6]
	Shin *et al*		[80]
	Al-Awadhi *et al*		[81]
		Tong *et al*	[20]
		Beck *et al*	[21]
		O'Connor *et al*	[22]
		Sinclair *et al*	[23]
	Weinberg *et al*		[26]
HCV	Benova *et al*		[41]
VZV	Tomonari *et al*		[44]
	Patrick *et al*		[45]
	Vandenbosch *et al*		[47]
HHV-6	D'Agaro *et al*		[53]
		Scheurer *et al*	[48]
		Yamane *et al*	[49]
		Hill *et al*	[50]
		Tomonari *et al*	[51]
		Sashihara *et al*	[52]
HHV-7	Abedi *et al*		[8]
HHV-8	Golchin *et al*		[7]
EBV	Hassan *et al*		[62]
	Haut *et al*		[63]
	Ohga *et al*		[64]
	Reddiconto *et al*		[65]
		Auger *et al*	[61]
		Barker *et al*	[67]
		Blaes *et al*	[69]
		Brunstein *et al*	[70]
		Dumas *et al*	[71]
		Kalra *et al*	[72]
AVs		Robin *et al*	[79]

UCBT: Umbilical cord blood transplantation; CMV: Cytomegalovirus; HCV: Hepatitis C virus; VZV: Varicella-zoster virus; HHV-6: Human herpesvirus-6; HHV-7: Human herpesvirus-7; HHV-8: Human herpesvirus-8; EBV: Epstein-Barr virus; AVs: Adenoviruses.

The initial infection is generally asymptomatic or associated with mild flu-like symptoms. In rare cases, it may cause a serious end-organ disease or systemic syndrome, either early or late period after transplantation with a poor prognosis. In some cases of congenital infections, CMV causes severe and permanent consequences such as sensorineural hearing loss, growth retardation, intellectual disability, and even death nevertheless, there are no effective interventions to interrupt the intrauterine transmission[16,19].

CMV infection can indirectly increase the risk of transplant-related mortality (TRM) by mediating the immunosuppressive effects. In this context, CMV has been related to the development of GVHD and bacterial or fungal superinfection, particularly in CMV-seronegative patients who received seropositive allografts[19,20].

Despite the advances in current preventive antiviral strategies and sensitive diagnostic techniques such as PCR-based assays, CMV remains the important cause of serious viral infections in the recipients of UCBT, as well as in allogeneic marrow or peripheral blood SCT. In this way, CMV reactivation rate following UCBT is noted to be 21%-100% and is similar when compared to peripheral blood or bone marrow SCT[21].

It has been reported that up to 30%-40% of seronegative pregnant women who infected by CMV transmit the virus to their fetus, suggesting a high incidence of cord blood contamination by CMV[16]. It has been shown that CMV can establish a lifelong

latency in hematopoietic progenitors and monocytes. Therefore, the virus might be transmitted by these infected cells to the immunocompromised recipient and then become reactivated[22,23] (Table 1). Pergam *et al*[24] indicated that high allograft white blood cell count is an important risk factor associated with CMV transmission due to the role of myeloid cells as a reservoir of latent CMV. In this context, Abedi *et al*[6] analyzed 825 UCB-derived buffy coat samples and reported that 17 samples have been positive for CMV latent infection.

The serostatus of the donor and recipient is the most important risk factor for CMV disease in allo-HSCT recipients. In this regard, CMV-seropositive recipients have been identified to be highly susceptible to developing CMV infection and CMV complications are primarily associated with viral reactivation. Seronegative patients who receive seropositive allografts are also susceptible to CMV transmission. As mentioned above, the risk for transmission of latent CMV from a CMV-seropositive donor to a CMV-seronegative patient is relatively low, but it increases TRM, mainly due to an increased risk for severe bacterial or fungal superinfection[24,25]. Therefore, for a CMV-seronegative recipient, it is preferable to select a CMV-seronegative donor to reduce the possibility of CMV transmission through allograft. On the contrary, using a seropositive donor for a seropositive recipient will probably result in a better outcome. This fact may be related to the transfer of primed CMV-specific T cells present in the allograft to the recipient[24].

Since the pediatric recipients of UCB transplant are primarily CMV-seronegative, CMV transmission by allograft is often of more importance than reactivation of the latent virus in the recipient[24,26]. Therefore, excluding the UCB donations from CMV seropositive mothers might be effective to prevent UCB-related CMV transmission.

Hepatitis B virus

Hepatitis B virus (HBV) is a double-stranded DNA virus, classified in the Hepadnaviridae family. Chronic HBV infection is a serious problem of public health affecting over 240 million people worldwide[27].

In the immunocompetent host, HBV infection is responsible for acute hepatitis, which may progress to chronic infection and lead to cirrhosis or hepatocellular carcinoma. Most HBV carriers, however, may never experience severe liver complications during their lifetime. While the risk of acquiring HBV infection *via* blood transfusion is nowadays extremely low, allogeneic HSCT patients still represent a high-risk group, being susceptible to be infected due to the lack of efficient immunity given both the disease and receiving the conditioning regimen before the transplantation. The prevalence of HBV infection in these patients ranges from 1% to 28%, according to geographic areas. The results of a multicenter study showed that the risk of HBV reactivation, two years after HSCT was 81% for allogeneic and 66% for autologous cases. Patients undergoing HSCT can also develop a de novo HBV infection following the transplantation. The risk of HBV transmission to uninfected recipients of bone marrow transplantation (BMT) is not 100% and the exact risk remains unclear[28,29].

Huang *et al*[30] exposed UCB-derived HSCs to HBV and demonstrated that HBV not only can infect these cells but also can replicate in them, and then suggested the possible role of HSCs as extrahepatic HBV reservoir. On the other hand, other studies have shown the risk of intrauterine transmission of HBV *via* peripheral blood mononuclear cells in addition to transplacental leakage and placental infection. These findings suggest the possibility of HBV transmission by UCB mononuclear cells to the recipient and highlight the importance of routine screening of UCB units[31,32]. To the best of our knowledge, very little published data are available about the prevalence and risk factors for HBV transmission by HSC transplant from UCB source.

Hepatitis C virus

Hepatitis C virus (HCV) is a double-stranded RNA virus of the Flaviviridae family. Global incidence of chronic HCV infection is about 170 million people and approximately 3-4 million more are infected each year[29,33]. As for HBV, patients infected with HCV show a mild to moderate liver disease on long-term monitoring depending on age at infection and host immune response[34].

HCV infection in HSCT recipients might be because of both virus reactivation and de novo infection. HCV reactivation after immunosuppressive therapy has led to fulminant hepatic failure in some cases. Accordingly, in a multicenter study by Locasciulli *et al*[35] the risk of HCV reactivation at 24 mo after HSCT has been 100% and 16% for allogeneic and autologous cases, respectively.

On the other hand, the rate of de novo HCV infection in HSCT recipients of donor-cell origin is controversial. In this context, 50% of the patients receiving an infected marrow became viraemic in a study by Locasciulli *et al*[36], while Shuhart *et al*[37] observed a 100% rate of virus transmission in such cases. Moreover, it has been

reported that HCV can infect HSCs and therefore, virus transmission from HCV-RNA positive donor to an uninfected recipient is possible[38].

HSCT has not a contraindication in HCV infected recipients without any evidence of liver damage. However, HCV-infected HSCT recipients are more prone to develop GVHD and fatal liver failure in comparison with non-infected recipients. Furthermore, outcomes in long-term survivors are significant, and they should be monitored carefully by regular examinations[39,40].

Anti-HCV positive but HCV-RNA negative donors are improbable to infect the recipients and may be selected for transplant donation for the patients without an alternative donor. Accordingly, all anti-HCV-positive donors should be tested for HCV-RNA. However, high-risk anti-HCV negative donors should also be tested for HCV-RNA[33,40].

The risk of vertical HCV transmission is lower than in HBV including 1.7% and 4.3% in children born to women positive for hepatitis C antibody or HCV-RNA, respectively. Despite the possibility of vertical HCV transmission from mother to fetus and possible contamination of UCB units, there is a paucity of published data that have focused on the possibility and outcomes of HCV transmission by UCBT. Future studies using molecular diagnostic methods and clinical monitoring will clarify the prevalence and importance of UCB-related HCV transmission[32,41].

Varicella-zoster virus

Varicella-zoster virus (VZV) or HHV-3 is an exclusively human alphaherpesvirus. The primary infection occurs typically as childhood chickenpox (varicella). As a common feature to all members of the Herpesviridae family, VZV is capable to establish latent infection in its host. It remains in a latent form for decades in cranial nerve ganglia and dorsal root ganglia, and then might become reactivated under the certain conditions. Reactivation of the virus, either spontaneously or following the post-transplant immunosuppression, may cause a painful and debilitating disease known as herpes zoster (shingles)[42,43].

The estimated prevalence of post-SCT VZV infection either primary infection or reactivation in children is as high as 22% to 32% after allogeneic and 9% to 46% after autologous transplantation. Based on previous studies, Older age, pre-transplant irradiation, HLA-mismatched transplantation, chronic GVHD, and recipient pre-transplant VZV seropositivity have been described as predisposing risk factors for VZV disease[44,45]. Accordingly, Umezawa et al.[46] retrospectively analyzed the clinical symptoms of VZV disease and risk factors for disease progression in allogeneic HSCT patients. They suggested that gender and total body irradiation did not affect the development of VZV dissemination, and concluded that delayed antiviral therapy is a serious risk factor for VZV dissemination following the allogeneic HSCT.

It has also been shown that VZV disease is more frequent and more severe after UCBT than other types of HSCT. In this regard, Tomonari[44] showed 80% cumulative incidence of VZV reactivation in adult patients who had undergone UCBT from unrelated donors. In another study, Vandenbosch and colleagues[47] compared the VZV reactivation rate in the total of 114 VZV seropositive children who had received UCBT or T-replete BMT and reported an incidence of 46% of VZV disease at 3 years after UCBT. This higher frequency in UCBT recipients may be related to delayed immune reconstitution after UCBT and therefore, necessitates the preemptive therapy or prophylaxis in these patients.

On the other hand, Patrick et al.[45] conducted a retrospective study to assess the efficacy of routine screening for identification of HSV or VZV viremia following HSCT. They aimed to discuss whether this screening identifies any patients with viremia who had not been identified via clinical manifestations. Finally, they concluded in agreement with the recommendation of the European Conference on Infections in Leukemia that routine screening for VZV is not obligatory in the pediatric HSCT recipients but regular clinical assessment should be performed.

HHV-6

HHV-6 belongs to the beta herpesviridae subfamily and exists as two closely related variants (A and B). Pathogenicity of HHV-6A is uncertain, whereas HHV-6B is the most frequent causative agent of HHV-6-related human diseases[48].

This virus is an opportunistic ubiquitous agent that infects most children in the early years of life. Primary infection is mainly associated with exanthema subitum (also called roseola infantum) and related febrile rash illnesses. Like the other herpesviruses, HHV-6 has the ability to persist in various cells of the host, especially in monocyte/macrophages and then become reactivated from latency during immunodeficiency, especially in HSCT recipients[26].

Several retrospective studies have shown the higher incidence of HHV-6 reactivation in the recipients of UCB than in patients receiving other stem cell sources,

and suggested to be related with high mortality rate and fatal complications including acute GVHD, bone marrow suppression, and CNS disease, especially the syndrome of post-transplantation acute limbic encephalitis called HHV-6-PALE[48,49]. Scheurer *et al*[48] conducted a systematic literature review and meta-analysis to investigate the prevalence and clinical significance of HHV-6 reactivation in UCBT recipients. They showed that prevalence of HHV-6 reactivation and related- encephalitis were significantly higher in UCB than non-UCB recipients, and emphasized the monitoring of UCB recipients for HHV-6 reactivation.

However, literature focusing on HHV-6 primary infection after UCBT and especially, HHV-6 transmission by UCB is scarce. Based on available data, HHV-6 DNA is detectable in plasma samples from 40% to 50% of HSC transplant recipients from adult donors and up to 80% of unrelated UCB recipients within 6 wk after transplantation[50]. Accordingly, Tomonari *et al*[51] have also shown the higher HHV-6 viral load using quantitative PCR in adult patients who underwent UCBT compared with unrelated BMT.

These reports in addition to the possibility of intrauterine transmission of HHV-6 and contamination of UCB cells suggest the possibility of HHV-6 transmission by UCB allograft and subsequent primary infection. This phenomenon might be associated with less efficient immunity against HHV6 in cord blood[52,53]. While more studies are needed to confirm and define the importance of UCBT in HHV-6 transmission, routine screening for HHV-6 and exclusion of PCR-positive UCB units seems to be efficient to prevent UCB-mediated virus transmission and related serious outcomes.

HHV-7

HHV-7 is a member of the beta herpesviridae family. Like HHV-6, it causes primary infection most commonly in infancy and childhood and is able to cause roseola. However, symptomatic HHV-7 infection is less common and occurs at a later age than with HHV-6. This virus remains latent in the human host and can become reactivated after transplantation. Right now, no clinical symptoms or significant laboratory abnormalities were found to be related to HHV-7 reactivation[54].

Owing to its selective tropism for CD4+ T lymphocytes and possibility of worsening the immunodeficiency state, the HHV-7 infection might be a serious threat in transplant recipients and impair the transplant engraftment. Mirandola *et al*[55] incubated cord blood CD34+ cells with HHV-7 and showed that HHV-7 affects the differentiation and survival of CD34+ hematopoietic progenitors. Consistently, Gonelli *et al*[56] showed that HHV-7 induces apoptosis of cord blood CD61+ megakaryocytic cells in vitro and may impair the development of megakaryocytic cells. Accordingly, Chan *et al*[57] noted the association of HHV-7 reactivation with delayed neutrophil engraftment following BMT. These findings are real causes for concern in patients with high risk of HHV-7 infection, such as HSCT patients.

Abedi *et al*[8] assayed a large number of UCB samples by quantitative real-time PCR and reported that 3.2% and 0.48% were positive for HHV-7 DNA in buffy coat and plasma as latent and active infections, respectively. In contrast, none of the samples were positive for HHV-7 DNA in the study by Weinberg[26].

Based on the high seroprevalence of HHV-7 in the general population and the role of this virus in myelopoiesis impairment, it seems that detection of HHV-7 in UCB donors could be a useful tool for prevention of UCB- associated HHV-7 transmission[55].

HHV-8

HHV-8, also called Kaposi sarcoma (KS)-associated herpesvirus, is a gamma-herpesvirus. Apart from KS, HHV-8 is the causative agent of lymphoproliferative disorders such as primary effusion lymphoma and multicentric Castleman's disease in immunosuppressed adults. HHV-8 has also been related to fatal hematopoiesis impairment in an autologous stem cell recipient[58,59].

The certain ways of HHV-8 transmission are unclear. Previous studies have suggested the sexual mode of virus transmission in homosexual men and horizontal transmission *via* saliva in endemic areas. Notably, HHV-8 from seropositive donor cell origin may be transmitted to the recipient[7,58].

Previous studies have indicated the minimum risk for vertical transmission of HHV-8 from mother to child during pregnancy, and therefore, the low seroprevalence of HHV-8 infection in UCB samples[7,26]. Accordingly, Golchin *et al*[7] surveyed a large number of UCB samples by real-time PCR and reported an only 1.38% HHV-8 prevalence in UCB mononuclear cells. However, HHV-8 has the ability to infect cord blood mononuclear cells and cause post-UCBT infection, and therefore it deserves the attention in UCBT settings[26].

Accordingly, defining the HHV-8 serostatus and avoiding matches between HHV-

8-positive donors and HHV-8-negative recipients appear to be effective to prevent virus transmission by UCBT in areas of high endemicity.

Epstein-Barr virus

Epstein-Barr virus (EBV) is a widespread gammaherpesvirus that infects over 90% of humans. In healthy individuals, EBV infection is tightly controlled by the immune system. After primary infection, EBV establishes a lifelong asymptomatic latent infection in B-cells of immunocompetent hosts. Later, immunosuppressive therapy given at HSCT may lead to EBV reactivation and subsequent EBV diseases, particularly life-threatening post-transplant lymphoproliferative disease (PTLD)[60,61]. Some studies have also reported the cases of UCB-transplanted patients who developed the EBV-related PTLD from graft-cell origin and proved the transmission of EBV infection by donor cells[62-65] (Table 1). EBV reactivation frequently occurs in patients having allogeneic HSCT and several risk factors for the development of EBV disease after HSCT have been reported, such as T-cell depletion, donor stem cell source, HLA mismatch, severe acute GVHD, EBV serostatus, the presence of CMV disease and possibly younger age[60,61].

Blood EBV DNA level has proven to be a predictive biomarker in allogeneic HSCT patients. In a clinical follow-up project, Li *et al*[61] evaluated the impact of EBV load on the survival of patients who had received transplant form different sources of stem cells, and found that patients with very low or high EBV-DNA load early after transplantation had a poor prognosis, compared to patients with intermediate levels.

Sundin and others have demonstrated that PTLD mostly originates from donor-derived cells, and risk for PTLD increases in positive donor/negative recipient (D+/R−) pairs. Therefore, selection of EBV-seronegative donors could reduce the risk of PTLD development[66-68]. There are also reports concerning the higher incidence of PTLD in patients who underwent UCBT compared with other HSC sources, especially when anti-thymocyte globulin is added to conditioning regimen[69,70]. Contrary to these findings, in a retrospective multicenter study, Dumas *et al*[71] studied 175 UCBT recipients for whom EBV RQ-PCR monitoring was performed, and concluded conversely that UCBT recipients are not more susceptible to EBV events if EBV load is regularly monitored and preemptive treatment performed.

Despite the low incidence of congenital EBV infection, the occurrence of EBV-associated PTLD is possible at least in unrelated UCBT setting and adds one additional fatal complication following UCBT. Therefore, EBV screening by sensitive and reliable tests may play an important role in the future evaluation of UCB units to use in transplantation[71,72].

Human adenoviruses

Human adenoviruses (AVs) are non-enveloped double-stranded DNA viruses that belong to the Adenoviridae family. AVs are divided into six subgroups (A through G) based on common biologic, immunologic, morphologic and genetic features[73].

In immunocompetent individuals, AV primary infection is mostly subclinical and self-limiting, although some severe courses have been described[74]. However, AV infection is more clinically important in patients with impaired immunity, particularly in HSCT patients and causes fatal complications. It is also more common to children than adults following the HSCT. In this regard, two studies compared the rates of AV isolation in children and adults after BMT and found 21% and 23% of children to be positive compared with 9% in adults, respectively[75,76].

In the allogeneic HSCT setting, AV infection can arise from *de novo* infection or reactivation of the latent endogenous virus. *De novo* infection can occur by transmission of the exogenous virus in D+/R− pairs. In this context, previous studies have demonstrated the 4-fold higher risk of primary AV infections in patients that received HSC graft from seropositive donors compared to seronegative ones. However, reactivation of endogenous latent AV seems to be the main cause of AV-associated fatal complication in immunocompromised patients[74,77,78].

Main risk factors predisposing an invasive AV infection include childhood, donor AV serostatus, severe GVHD, HLA-mismatched transplantation, CMV viremia, and T-cell depletion. Furthermore, UCBT is suggested to be an independent risk factor for AV infection probably due to the lack of mature lymphocytes in CB, as cellular components of antiviral defense[79].

Runde *et al*[77] studied the prevalence and risk factors of AV infection in allo-HSCT recipients and showed that AV antibody status of the donor had a strong impact on the development of AV infection in the recipients. Their finding supports indirectly the hypothesis that AV infection following HSCT is not always the result of virus reactivation, and the virus might be transmitted by infected cells from AV seropositive donors to the recipients. This hypothesis is proved if the same AV is detected by molecular analyses in donors and corresponding recipients.

To the best of our knowledge, there are few studies that have focused on the risk of AV transmission by UCB transplant compared to other HSC sources. However, the presence of AV DNA positive cells besides naivety of T cells serves UCB as a putative source of AV infection in the immunocompromised recipients.

CONCLUSION

The amount of threat for transmission of infections carried with allogeneic transplantation, notably of viruses, is largely unknown and difficult to assess. The approach to virological screening of UCB stem cell donors varies with national and regional regulations. Over recent years, UCBT has become a valuable alternative for patients who lack a suitably matched bone marrow donor. However, UCBT is associated with several limitations, in particular, the low number of mature lymphocytes and poor immune reconstitution. Given these limitations, virus transmission *via* UCB may cause serious infectious complication in the immunocompromised recipients, and therefore, excluding the viral-contaminated UCB units might be an effective policy to reduce the rate of UCBT-related infection and mortality. Taken together, complete prevention of the transmission of donor-derived viral pathogens in SCT is not possible. However, having the knowledge of the transmission route and the prevalence of viruses will improve the safety of transplantation.

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