Systematic Review

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Incidence of cancer after paediatric solid organ transplant recipients: A Scoping Review

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ABSTRACT

Background: To investigate the incidence of post-transplant malignancies in paediatric recipients of solid organ transplants.

Materials and Methods: We searched MEDLINE, Scopus and Web of Science up to January 2025 for observational studies reporting on cancer incidence in children who underwent solid organ transplantation (SOT). Data extraction and quality assessment were performed by two independent reviewers. Data on incidence rates, types of malignancies, and patient demographics were extracted and analysed.

Results: Sixteen studies with a total of 26,310 paediatric transplant recipients were included. The cumulative incidence of cancer after kidney transplantation ranged from 10.2% at 15 years to 27% at 25 years. For liver transplantation, the incidence was 22% at 25 years, with a range from 3.4% to 7.1% incidence of post-transplant lymphoproliferative disorders (PTLD). Following heart transplantation, the incidence was 30.5% at 10 years.

Conclusions: Paediatric solid organ transplant recipients face a significant risk of developing cancer, particularly PTLD. Regular monitoring and early intervention are essential for improving long-term outcomes.

Key Words: *Paediatric transplantation; cancer incidence; post-transplant lymphoproliferative disorders; prognosis; scoping review*

INTRODUCTION

Paediatric solid organ transplantation (SOT) stands as a cornerstone of modern medicine, offering a lifeline to children grappling with end-stage organ failure [1]. Among the organs transplanted most frequently in paediatric patients are the kidneys, liver, and heart [2]. These life-saving procedures have revolutionised the management of various paediatric conditions, providing hope for improved quality of life and long-term survival [2]. Despite the remarkable progress in paediatric SOT, the necessity for prolonged immunosuppressive therapy remains a significant challenge [3]. The heightened risk of rejection necessitates the use of potent immunosuppressive agents, which in turn predispose recipients to complications, including infections and malignancies [3]. The frequency of transplantation and the severity of underlying diseases contribute to the increased susceptibility to complications, underscoring the need for vigilant monitoring and tailored therapeutic strategies [4].

The immunocompromised state resulting from long-term immunosuppression makes paediatric solid organ

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transplant recipients particularly vulnerable to malignancies [5]. Extensive literature has documented an elevated incidence of various cancers in this population, ranging from skin cancers, such as squamous cell carcinoma and melanoma, to lymphomas and solid tumours affecting various organ systems [6-8]. Studies have highlighted the multifactorial nature of cancer development post-transplantation, implicating factors such as the intensity and duration of immunosuppression, viral infections, genetic predisposition, and environmental exposures [9], [10]. While transplantation extends life expectancy and enhances quality of life, the heightened risk of malignancy poses formidable challenges in paediatric transplant care [6]. The prevalence of malignancies in paediatric patients following SOT represents a significant clinical challenge.

Paediatric solid organ transplant recipients face a spectrum of malignancies, ranging from skin cancers to lymphomas and solid tumours [11]. The incidence and types of cancer vary depending on factors such as the type of transplanted organ, duration of immunosuppressive therapy, and age at transplantation [12]. In this scoping review the authors aim to conduct a comprehensive analysis of the incidence and types of post-transplant malignancies in paediatric recipients of kidney, liver, and heart transplants.

METHODS

This scoping review has been reported in accordance with the Preferred Reported Items for Systematic Review and Meta-Analysis (PRISMA) statement [13].

Data sources

A systematic search was conducted in MEDLINE (via PubMed), Scopus and Web of Science up to 1 January 2025. The search strategy is presented in Supplementary Table 1. Keywords included «paediatric», «solid organ transplant», «cancer» and «malignancy".

Study Selection

Observational studies in the paediatric population (under 18 years) who had undergone kidney, liver, or heart transplantation and documented the incidence of malignancies were included in the present study. Exclusion criteria included studies focusing solely on adult populations, case reports, and reviews without original data. After removing duplicate entries, two independent reviewers (A.S. and G.S.) screened the titles and abstracts of all retrieved articles. Full-text versions of potentially relevant studies were then assessed according to predefined

TABLE 1. Occurrence of malignancy after kidney transplantation.

	Study	Transplant Year	Average Transplant Age	No. of Patients	No. of Kidneys (%)	No. of Cancers (%)	Average Cancer Age	Cancer Type (N)	Cumulative Incidence
Solid organ transplantation	Kitchlu 2019 [18]	1/7/1991 - 31/12/2014	NA	951	400 (42)	25 (6)	18.7	NA	NA
	Enden 2020 [19]	1/1/1982 - 31/12/2015	7.9	233	137	14 (10.2)	18.7	NHL (10)	NA
	Yanik 2017 [17]	1987 - 2011	NA	17,958	7,822 (43.6)	102	NA	NHL	NA
	Debray 2009 [7]	1/1996 - 7/2007	10.6	1,326	505 (38)	17	NA	PTLD (15)	NA
	Simard 2011 [16]	1970 - 2007	11.66	536	330	26	27.4	Non-melanoma skin (7)	NA
Kidney transplantation	Francis 2017 [14]	1/1963 - 12/2013	NA	NA	1,734	289 (16.7)	14.7	Non-melanoma skin (196)	27% at 25 years
	Ploos van Amstel 2015 [22]	1972 - 2010	13.23	NA	249	54	33.5	Non-melanoma skin (40)	41% at 30 years
	Yabuuchi 2021 [21]	1983 - 2016	11.43	NA	356	12 (3.4)	18.5	PTLD (5)	14.7% at 30 years
	Koukourgianni 2009 [20]	4/1987 – 3/2007	9.7	NA	219	16 (7.3)	NA	PTLD (10)	10.2% at 15 years

Abbreviations: Non-Hodgkin lymphoma, NHL; Posttransplant Lymphoproliferative Disorders, PTDL

eligibility criteria, considering only publications in English. Any discrepancies were resolved through consensus or by consulting a third reviewer (G.T.).

Data extraction

Data was extracted independently by two reviewers (A.S and G.S.) using a data extraction form in Microsoft Excel. The population demographics included the type of organ transplanted (kidney, liver, or heart), with a focus on paediatric patients under 18 years of age. The incidence of malignancies was recorded across the three organ types, with each study presenting the total number of patients (n) and the corresponding percentages (%) for cancer incidence where applicable. Additionally, the mean age at transplantation was noted for each study, with values reported in years. The statistical representation of the cancer data was presented through absolute numbers (n) for the incidence of specific cancers and percentages (%) to denote the prevalence of each malignancy within the study populations. Furthermore, the studies also provided cumulative incidence rates, with cancer types categorised by organ system.

RESULTS

Search results and study characteristics

The flow diagram depicting the study selection process is presented in Figure 1. From the initial search, 1,445 articles were identified. All articles underwent title and abstract screening. Thirty-one studies were retained for full-text assessment. Sixteen studies did not meet the

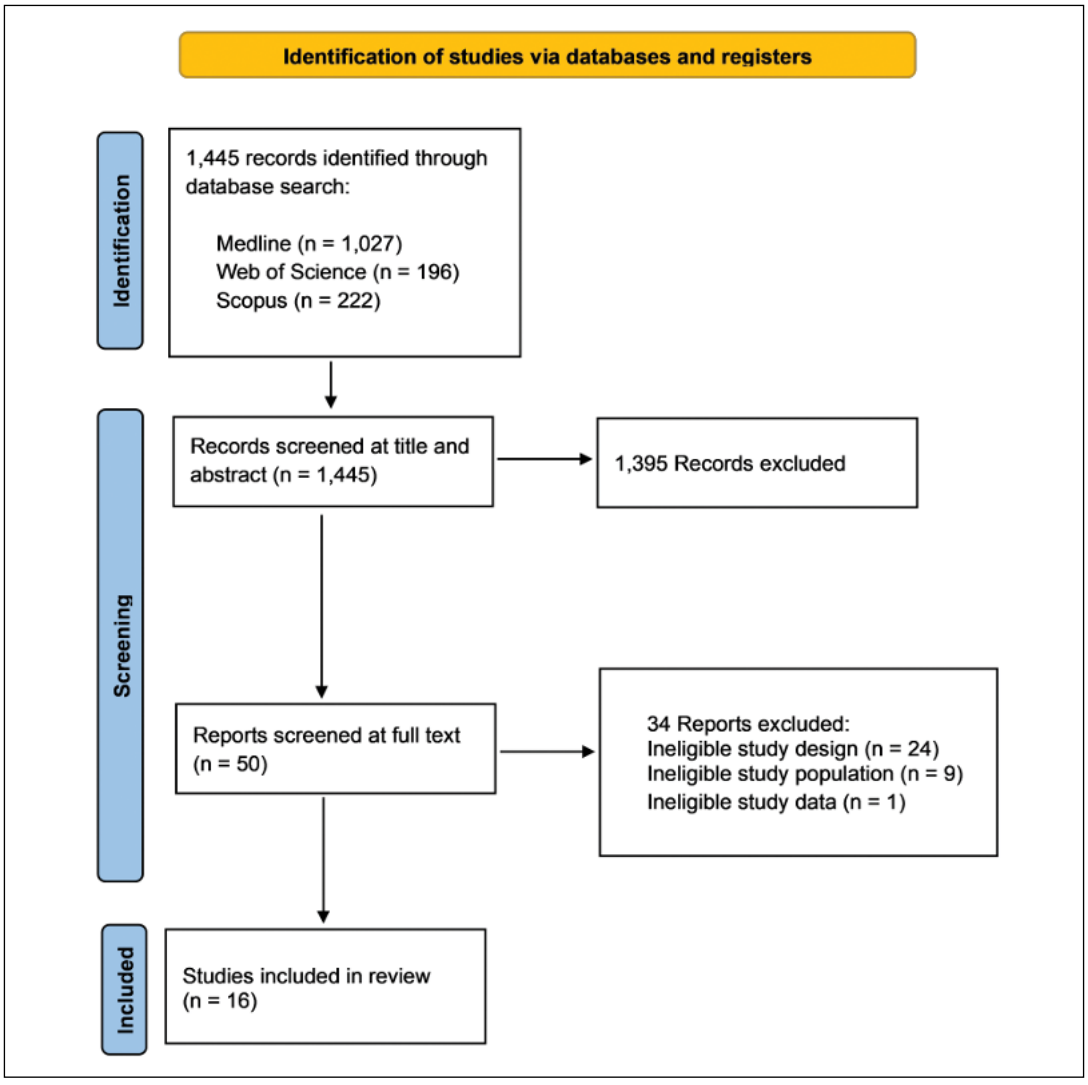

FIGURE 1. Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow chart for the identification inclusion and exclusion of studies.

inclusion criteria and were subsequently excluded. Finally, sixteen observational studies were selected for the scoping review [7,14-28]. Five studies evaluated the risk of malignancy in paediatric patients post SOT [7,16-19], four after kidney transplantation [14,20-22], three after liver transplantation [15,24,25] and one after heart transplantation [23]. Three studies specifically assessed the risk of post-transplant lymphoproliferative disorders (PTLD) following heart [26,27] and liver [28] transplantation in paediatric populations. In total, 26,310 paediatric patients were included across the fifteen studies. All data were extracted from registries.

Malignancy post kidney transplantation

Data from nine studies were utilised to assess the occurrence of malignancy following kidney transplantation in paediatric patients [7,14,16-22]. Data is presented in Table 1. Specifically, the study by Kitchlu et al. (2019) includes data from 1991 to 2014 [18]. Out of 951 individuals undergoing SOT, 42% developed cancer, with a mean age of cancer onset at 18.7 years. In the study by Enden et al. (2020), lasting from 1982 to 2015, with a mean transplantation age of 7.9 years, out of 233 individuals examined, 10.2% developed cancer, predominantly lymphomas (NHL), with a mean age of cancer onset at 18.7 years [19]. The study by Yanik et al. (2017) includes data from 1987 to 2011 [17]. Out of 17,958 individuals examined, 43.6% developed cancer, with the majority suffering from NHL. The study by Debray et al. (2009) includes data from 1996 to 2007, with a mean transplantation age of 10.6 years [7]. Out of 1,326 individuals examined, 38% developed cancer, with PTLD being the predominant cancer type. The study by Simard et al. (2011) includes data from 1970 to 2007, with a mean transplantation age of 11.66 years [16]. Out of 536 individuals examined, 26% developed cancer, with the majority having non-melanoma skin cancer. The study by Francis et al. (2017) includes data from 1963 to 2013, without reference to the mean transplantation age [14]. Out of 1,734 individuals examined, 16.7% developed cancer, with the majority having non-melanoma skin cancer. The study by Ploos van Amstel et al. (2015) includes data from 1972 to 2010, with a mean transplantation age of 13.23 years [22]. Out of 249 individuals examined, 21.7% developed cancer, with the majority having non-melanoma skin cancer. The study by Yabuuchi et al. (2021) includes data from 1983 to 2016, with a mean transplantation age of 11.43 years [21]. Out of 356 individuals examined, 3.4% developed cancer, with PTLD being the predominant cancer type. Lastly, the study by Koukourgianni et al. (2009) includes data from 1987 to 2007, with a mean transplantation age of 9.7 years [20]. Out of 219 individuals examined, 7.3% developed cancer, with PTLD being the predominant cancer type.

Malignancy post liver transplantation

Eight studies were utilised to evaluate the likelihood of malignancy following liver transplantation in paediatric patients [7,15,16,18,19,24,25,28]. Data is presented in Table 2. Specifically, the study by Kitchlu et al. (2019) reports that out of 951 individuals examined, 30% underwent liver transplantation, while 7% developed cancer, with a mean age of cancer onset at 9.2 years [18]. In the study by Enden et al. (2020), out of 233 individuals examined, 3.8% developed cancer, with B-cell lymphoma being the predominant cancer type [19]. The study by Debray et al. (2009) reports that out of 1,326 individuals examined, 45% underwent liver transplantation, while 42% developed cancer, with PTLD being the predominant cancer type [7]. The study by Simard et al. (2011) reports that out of 536 individuals examined, 24% underwent liver transplantation, while 6% developed cancer, with NHL being the predominant cancer type [16]. The study by Aberg et al. (2008) includes data from 1982 to 2005 [25]. Out of 78 individuals examined, 6% developed cancer, with non-melanoma skin cancer being the predominant cancer type. The study by Aberg et al. (2018) includes data from 1982 to 2013 [15]. Out of 923 individuals examined, 14% developed cancer, with NHL being the predominant cancer type. The study by Karakoyun et al. (2017) includes data from 1997 to 2015, with a mean transplantation age of 5.4 years [24]. Out of 206 individuals examined, 13% underwent liver transplantation, and PTLD was the predominant cancer type. Lastly, the study by Dogan et al. (2024) reports on 112 paediatric liver transplant recipients. Among them, 43.75% developed EBV DNAemia, and 16.3% developed PTLD [28]. The predominant PTLD subtype was EBV-related B-cell lymphoma, while the mean time to PTLD diagnosis was 41.3 months post-transplant [28].

Malignancy post heart transplantation

Seven studies were utilised to assess the likelihood of malignancy following heart transplantation in paediatric patients [7,16,18,19,23,26,27]. Data is presented in Table 3. Specifically, the study by Kitchlu et al. (2019) reports that out of 951 individuals examined, 23% underwent heart transplantation, while 14% developed cancer [18]. In the study by Enden et al. (2020), out of 233 individuals examined, 4.7% developed cancer, with NHL being the predominant cancer type [19]. The study by Debray et al. (2009) reports that out of 1,326 individuals examined, 8% underwent heart transplantation, while 4% developed cancer, with PTLD being the predominant

TABLE 2. Occurrence of malignancy after liver transplantation.

	Study	Transplant Year	Average Transplant Age	No. of Patients	No. of Livers (%)	No. of Cancers (%)	Average Cancer Age	Cancer Type (N)	Cumulative Incidence
Solid organ transplantation	Kitchlu 2019 [18]	1/7/1991 - 31/12/2014	NA	951	283 (30)	19 (7)	9.2	NA	NA
	Enden 2020 [19]	1/1/1982 - 31/12/2015	4.9	233	53	2 (3.8)	18.6	B-cell lymphoma (1) - Skin (1)	NA
	Debray 2009 [7]	1/1996 - 7/2007	4.4	1,326	605 (45)	42	NA	PTLD (34)	NA
	Simard 2011 [16]	1970 - 2007	11.66	536	128	6	27.4	NHL (5)	NA
Evaluation of PTLD	Dogan 2024 [28]	2010 - 2022	5.3	NA	112	8 (16.3)	NA	PTLD	7.1%
Liver transplantation	Aberg 2008 [25]	1982 - 2005	NA	NA	78	2 (6)	NA	Non-melanoma skin	NA
	Aberg 2018 [15]	1982 - 2013	NA	NA	923	37	NA	NHL (14)	22% at 25 years
	Karakoyun 2017 [24]	1997 - 2015	5.4	NA	206	13	8.6	PTLD (7)	3.4%

Abbreviations: Non-Hodgkin lymphoma, NHL; Posttransplant Lymphoproliferative Disorders, PTDL

cancer type [7]. The study by Simard et al. (2011) reports that out of 536 individuals examined, 11.4% underwent heart transplantation, while 4% developed cancer, with NHL being the predominant cancer type [16]. The study by Webber et al. (2006) includes data from 1993 to 2002, with a mean transplantation age of 6.1 years [26]. Out of 1,184 individuals examined, 8.2% developed cancer. The study by Arshad et al. (2019) includes data from October 1992 to October 2018, with a mean transplantation age of 5.6 years [27]. Out of 202 individuals examined, 11.9% underwent heart transplantation, while 9.9% developed cancer. The above two studies specifically evaluated the

TABLE 3. Occurrence of malignancy after heart transplantation.

	Study	Transplant Year	Average Transplant Age	No. of Patients	No. of Hearts (%)	No. of Cancers (%)	Average Cancer Age	Cancer Type (N)	Cumulative Incidence
Solid organ transplantation	Kitchlu 2019 [18]	1/7/1991 - 31/12/2014	NA	951	218 (23)	30 (14)	NA	NA	NA
	Enden 2020 [19]	1/1/1982 - 31/12/2015	10.3	233	43	2 (4.7)	17.3	NHL (2)	NA
	Debray 2009 [7]	1/1996 - 7/2007	8.6	1,326	104 (8)	4	NA	PTLD (4)	NA
	Simard 2011 [16]	1970 - 2007	11.66	536	61	4	27.4	NHL (3)	NA
Evaluation of PTLD	Webber 2006 [26]	1993 - 2002	6.1	NA	1,184	56	8.2	PTLD	NA
	Arshad 2019 [27]	10/1992 - 10/2018	5.6	NA	202	24 (11.9)	9.9	PTLD	30.5% at 10 years
Heart transplantation	Gambino 2007 [23]	11/1985 - 1/2005	9.7	NA	43	15	NA	PTLD (8)	NA

Abbreviations: Non-Hodgkin lymphoma, NHL; Posttransplant Lymphoproliferative Disorders, PTDL

occurrence of PTLD. Lastly, the study by Gambino et al. (2007) includes data from November 1985 to January 2005, with a mean transplantation age of 9.7 years [23]. Out of 43 individuals examined, 15% underwent heart transplantation, and PTLD was the predominant cancer type in the study.

DISCUSSION

In this scoping review we evaluated the frequency for cancer occurrence following SOT in the paediatric population. Summarily, the results indicate a significant association between transplantation and cancer occurrence, with 819 patients overall developing cancer out of 26,310. The main types of cancer reported include PTLD, particularly NHL, and non-melanoma skin cancers. Following kidney transplantation, the cumulative incidence ranges from 10.2% after 15 years to 27% after 25 years, after liver transplantation, a 22% incidence is reported after 25 years, and a range from 3.4% to 7.1% incidence regarding the likelihood of PTLD development, and finally, after heart transplantation, a 30.5% incidence is reported after ten years. The likelihood of cancer occurrence post kidney transplantation increases over time, while the risk of cancer occurrence is significantly higher post heart transplantation.

The data from the scoping review confirm the overall trend presented in the literature review. Based on the research data, an increase in cancer risk is significant, with some studies reporting an even greater risk in paediatric patients compared to adults [6,29,30]. The type of cancer varies, with common types being non-melanoma skin cancers and PTLD [6]. Additionally, the average age of cancer onset after transplantation is significantly younger compared to general populations, making monitoring and prevention of malignancy even more critical for transplant recipients [17,29].

Immunosuppression is a critical part of transplant therapy, as it helps prevent rejection of the transplanted organ [31]. However, continuous immunosuppression may have adverse effects, including an increased risk of cancer occurrence [31]. Excessive suppression of the immune system, especially over time as seen in paediatric transplantations, may allow cancer cells to develop and further spread, as the normal mechanisms for controlling cancer cells are compromised [32]. This can lead to the development of lymphomas, non-melanoma skin cancers, and other types of cancer [32]. Additionally, immunosuppression may affect the action of normal immune cells that fight cancer cells, making the body's response to cancer more difficult and allowing cancer cells to further spread [5,10]. Therefore, immunosuppression presents a double-edged impact: on one hand, it protects the transplanted organ from rejection, but on the other hand, it may increase the risk of cancer occurrence.

Paediatric transplant patients also face various other factors that can lead to cancer occurrence. Besides immunosuppression, other factors influencing cancer risk include genetic predisposition, pre-existing infections, exposure to carcinogens, and disruptions of the immune system [33]. Transplant recipients, due to the need for long-term pharmacological treatment and immunosuppression, are susceptible to increased exposure to carcinogens and immune system disruptions, which can create an environment conducive to cancer development [34]. Research data confirm that transplant patients have an increased risk of cancer compared to the general population [30]. Additionally, it is observed that cancer occurrence post-transplantation is more common in specific organs, such as the kidney and heart, compared to others [35].

When cancer is discovered in children following transplantation, management usually takes a comprehensive strategy based on the type and stage of cancer, as well as the patient's condition. Therapeutic options may include surgical intervention, chemotherapy, radiotherapy, and in some cases, immunotherapy or outcome-based therapy [6,17]. It is essential to consider the child's sensitivity due to their young age and tailor the treatment accordingly [33]. The prognosis after cancer occurrence post SOT in paediatric patients depends on various factors, including the type of cancer, disease stage, selected treatment, and overall health status of the patient [36]. Early diagnosis and appropriate treatment can significantly improve survival prospects [37]. However, the prognosis may be poorer compared to adults due to the young age of patients, their sensitivity to treatment, and the potential recurrence of cancer [14,22]. Prognosis also depends on the ability to respond to treatment and manage complications, such as graft rejection and immunosuppression-related complications [22]. Additionally, prognosis is influenced by the presence of potential transplantation complications, such as graft dysfunction or the development of other new diseases [19].

The present study has several limitations that should be considered. Although the participants were numerous overall, the search strategy yielded only 1,445 studies, and data heterogeneity limited the generalisability of findings. Future research should adopt broader search strategies and standardised reporting methods to improve data comparability. Additionally, many studies lacked critical variables, such as the average age of transplantation or detailed immunosuppression protocols, making interpretation and clinical implementation challenging. While these findings should be applied with caution due to the quality and variability of the included studies, they highlight the importance of targeted monitoring for high-risk paediat-

ric transplant recipients. Future studies should focus on standardising methodologies, conducting multi-center comparative analyses, and extending follow-up durations to better understand late-onset malignancies and improve clinical care for this vulnerable population.

In summary, the present scoping review evaluated the likelihood of malignancy occurrence post SOT in paediatric patients. The results of the review highlighted the high rate of cancer occurrence post transplantation, with lymphatic system cancers being the most frequent type in this population group. Additionally, it was observed that paediatric patients undergoing SOT face challenges regarding the occurrence and management of cancer, often requiring careful monitoring and tailored treatment. Future studies are recommended to systematically assess this risk, conducting statistical synthesis of the data.

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Data availability: *The data that support the current study are available from the corresponding author upon reasonable request.*

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