RESEARCH ARTICLE

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Factors Impeding the Timely Pathologic Diagnosis of Malignant Small Round Blue Cell Tumors in a Pediatric Tertiary Care Center in the Philippines: Identifying Opportunities to Optimize Pediatric Cancer Management

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Abstract

Objective: This study aimed to evaluate the turnaround time (TAT) of histopathology reports for pediatric small round blue cell tumors (PSRBCTs) at the largest pediatric tertiary care center in the Philippines, and to identify the factors affecting TAT. Additionally, the reasons for the inability to accurately diagnose cases were investigated. **Methods:** A retrospective cross-sectional study was conducted on 232 tumor cases from 2018 to 2022. The overall mean TAT, as well as the TAT for specific phases (pre-analytical, analytical, and post-analytical), was determined. Factors contributing to delays in diagnosis were analyzed. Multivariate analysis was used to assess associations between these factors, and Spearman correlation was applied to explore the relationship between the number of consultant pathologists who reviewed a case and the mean TAT. **Result:** The overall mean TAT for PSRBCT histopathology reports was 13.39 days. The pre-analytical, analytical, and post-analytical phases had TATs of 1.89, 11.56, and 4.53 days, respectively. Unavailability of immunohistochemical stains significantly increased TAT (95% CI, p-value < 0.01). A significant reduction in TAT was observed during the COVID-19 pandemic (95% CI, p-value < 0.01). A direct correlation was found between the number of consultant pathologists reviewing a case and the mean TAT (95% CI, p-value < 0.01). The main barrier to rendering a specific diagnosis was the lack of access to molecular tests. **Conclusion:** Prolonged TAT reflects underlying issues that delay the accurate diagnosis of PSRBCTs. The identified deficiencies, including limited access to ancillary tests and specialized expertise, offer opportunities to improve pediatric cancer care in the Philippines.

Keywords: Pediatrics- small round blue cell tumors- histopathology- global health- quality assurance- turnaround time

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Introduction

Pediatric small round blue cell tumors (PSRBCTs), which predominantly affect children, are a group of malignant neoplasms that exhibit poor or absent cytologic differentiation. These tumors share similar histomorphologies, earning them the "small round blue cell tumors" designation [1]. Classic examples include rhabdomyosarcoma, neuroblastoma, lymphoma, Ewing sarcoma, and Wilms tumor, among others [1]. Though classified under one umbrella, each tumor type has a distinct cellular origin, which demands a specific management approach, underscoring the importance of an accurate diagnosis. In the Philippines, there were 12,765 documented cases of PSRBCTs from 2018-2022, with a mortality rate of 5.3% [2]. At the Philippine Children's Medical Center (PCMC), the largest children's hospital providing pediatric care in the country, PSRBCTs account for 16% of all pediatric cases, 32% of neoplastic cases, and 55% of malignant cases during the same period [3].

PSRBCTs can be difficult to diagnose, often requiring consensus from a team of pathologists, especially in resource-limited regions. Diagnostic delays can lead to treatment postponements and higher morbidity [4]. In the United States, pediatric oncologists rely on final pathology reports before starting treatment, thus the need for an accurate and expeditious diagnosis. Turnaround time (TAT) of the pathologic diagnosis, the period from specimen receipt to the release of the final pathology report, serves as a key measure of diagnostic efficiency and is critical for timely patient management. TAT not only impacts timely treatment but also affects patient and family

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satisfaction, hospital costs, and quality assurance [4]. Studies indicate that general TAT for surgical pathology cases varies widely, with some developing countries taking 2 to 71 days [5-6]. However, few studies have focused on large or complex specimens, such as those from malignant tumors [7]. To date, only one Philippine-based study has investigated TAT in surgical pathology [8]. Delays in TAT can be due to various factors including inadequate clinical information, prolonged fixation times, limited access to certain special stains and immunohistochemistry (IHC), and consultations [9]. Delayed diagnoses have been linked to increased mortality, particularly in low- and middle-income countries [10]. Additionally, the availability of advanced techniques, which can have prognostic implications for PSRBCTs, is often limited in resource-constrained settings [11].

This study aimed to investigate the TAT of PSRBCT histopathologic reports at a pediatric tertiary-care center in the Philippines from 2018 to 2022. Specifically, it assessed the mean TAT during the pre-analytical, analytical, and post-analytical phases, identified variables affecting TAT, and explored the causes of diagnostic delays.

Materials and Methods

This retrospective cross-sectional study included all resections and biopsies of PSRBCTs diagnosed for the first time at the Philippine Children's Medical Center (PCMC) from 2018 to 2022. The tumors considered PSRBCTs for this study were listed in Table 1. They were based on a more comprehensive inclusion approach, as definitions of PSRBCTs vary across institutions and literature. Excluded were referral cases for slide review, non-primary in-house diagnoses (e.g., residual tumors, recurrences, or metastasis), and cases lacking necessary information to calculate TAT.

Clinical and pathological data were obtained from histopathology reports accessed via the Laboratory Information System and archived electronic copies of supplemental reports. Temporal data, such as IHC stain billing dates, were retrieved from the Histopathology section and Laboratory reception records. The data was tabulated and encoded in Microsoft Excel. Frequency and ranges were reported, with checks for normality to remove outliers before analysis. The data, excluding 28 outliers with extreme turnaround times (Table 2), was used to compute the overall mean TAT and TAT for each phase, divided into the pre-analytical, analytical, and post-analytical phases. A diagram of the overall workflow from specimen receipt to case sign-out is outlined in Figure 1. For analyzing the COVID-19 pandemic as a contributing factor, TAT from 2018-2019 was compared with the TAT from 2020-2022. Multiple linear regression was used to assess associations between mean TAT and factors including additional processing techniques, specimen regrossing, IHC stains performed at external labs, and the COVID-19 pandemic. Spearman correlation was used to evaluate the relationship between the number of consultants reviewing a case and the mean TAT.

Results

Demographics

Of the 272 primary PSRBCT surgical pathology cases from 2018 to 2022, 12 were excluded (resection specimens with prior biopsy diagnoses from either in-house or other institutions), and 28 were eventually determined to be outliers, leaving 232 cases suitable for analysis. The gender distribution was nearly equal, with 51.03% males and 48.97% females (male-to-female ratio: 1.04:1). The majority of patients were aged 1-3 years (41.44%), followed by 7-12 years (20.89%). A decreasing trend in PSRBCT cases was observed from 2018 to 2022. The most common diagnoses were Wilms tumor (13.36%), retinoblastoma (12.93%), neuroblastoma (10.34%), and lymphoblastic lymphoma (10.34%) (Table 1).

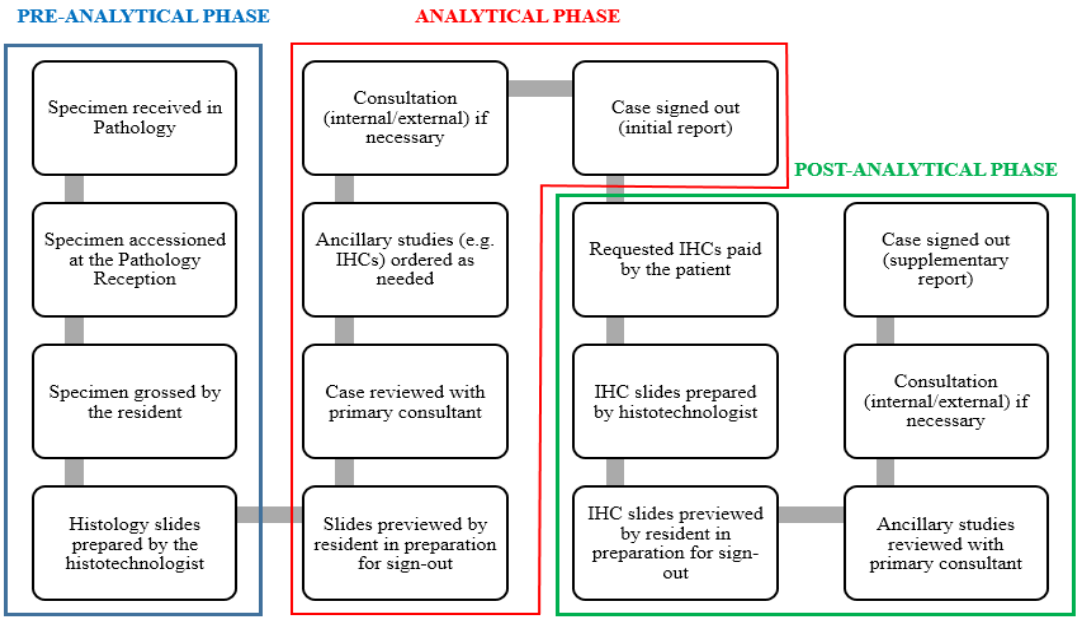

Figure 1. PCMC Workflow in the Diagnosis of Small Round Cell Tumors

Table 1. Turnaround Time (TAT) by Diagnosis

Diagnosis	N	Frequency (%)	Mean TAT ± SD (days)	TAT Range	Mean, SD and Range of Consultants per case
Wilms Tumor	31	13.36	9.16 ± 4.55	3 – 26	3.23 ± 1.60 (2-9)
Retinoblastoma	30	12.93	11.87 ± 2.90	6 – 16	2.2 ± 0.48 (2-4)
Neuroblastoma	24	10.34	13.13 ± 5.65	4 – 23	4.5 ± 1.87 (2-9)
Lymphoblastic Lymphoma	24	10.34	16.67 ± 7.36	5 – 31	3.25 ± 1.64 (1-8)
Rhabdomyosarcoma	23	9.91	13.74 ± 5.31	4 – 22	4.78 ± 1.84 (2-8)
Hepatoblastoma	22	9.48	9.73 ± 5.53	2 – 24	2.5 ± 0.84 (2-5)
Medulloblastoma	18	7.76	13.44 ± 5.43	5 – 26	1.78 ± 0.53 (1-3)
Burkitt Lymphoma	7	3.02	15.14 ± 3.44	9 – 19	3.57 ± 1.5 (2-7)
Anaplastic Large Cell Lymphoma	5	2.16	19.2 ± 5.95	11 – 27	3 ± 1.10 (2-5)
Germinoma and Dysgerminoma	5	2.16	15.6 ± 7.58	7 – 29	1.4 ± 0.49 (1-2)
Rhabdoid Tumors	4	1.72	23 ± 5.24	19 – 32	4.5 ± 2.60 (2-8)
Diffuse Large B Cell Lymphoma	3	1.29	17.33 ± 5.79	11 – 25	4 ± 1.41 (3-6)
Desmoplastic Small Round Cell Tumor	2	0.86	20 ± 2	18 – 22	5.33 ± 2 (3-7)
Synovial Sarcoma	2	0.86	15 ± 1	14 – 16	6.5 ± 0.5 (6-7)
CIC-rearranged Sarcoma	1	0.43	22	-	4
Myeloid Sarcoma	1	0.43	17	-	4
Melanotic Neuroectodermal Tumor of Infancy	1	0.43	11	-	3
Pleuropulmonary Blastoma	1	0.43	4	-	2
Tumors with incomplete work-up					
CD99+ malignant neoplasms (possibly Ewing and Ewing-like Sarcomas)	14	6.03	14.57 ± 7.75	5 – 28	5.21 ± 1.78 (2-9)
Non-Hodgkin Lymphoma, not otherwise specified	5	2.16	15 ± 6.69	4 – 22	4.6 ± 2.25 (3-9)
Small round cell tumor, not further characterized	5	2.16	14.8 ± 5.15	8 – 22	3.6 ± 1.2 (3-6)
Undifferentiated sarcoma	2	0.86	19.5 ± 2.5	17 – 22	10 ± 2 (8-12)
Germ Cell Tumor, not otherwise specified	2	0.86	15 ± 8	7 – 23	6.5 ± 0.5 (6-7)
Total	232	100	13.39 ± 6.30	2 – 32	3.54 ± (1-12)

Of the 28 outliers, 9 (32.14%) are medulloblastoma cases, followed by 4 (14.29%) cases of Wilms tumor and 4 (14.29%) cases of diffuse large B cell lymphoma (14.29%) cases. The case with the longest turnaround time (TAT) was a diffuse large B-cell lymphoma (109 days). The longest interval within this case occurred 66 days between the initial report, when immunohistochemical (IHC) studies were requested, and the time these studies were paid for and charged.

Turnaround Time (TAT) and Factors Affecting TAT

The mean TAT for diagnosing PSRBCTs was 13.39

Table 2. Outliers and Their Turnaround Times

Diagnosis	N	Frequency (%)	Mean TAT ± SD (days)	TAT Range
Medulloblastoma	9	32.14	42.56 ± 8.63	33 - 58
Wilms Tumor	4	14.29	69.75 ± 23.5	49 - 108
Diffuse Large B Cell Lymphoma	4	14.29	64.25 ± 26.24	43 - 109
Germinoma	2	7.14	47 ± 10	37 - 57
Neuroblastoma	1	3.57	40	40
Rhabdomyosarcoma	1	3.57	82	82
Myeloid Sarcoma	1	3.57	36	36
Burkitt Lymphoma	1	3.57	34	34
Desmoplastic Small Round Cell Tumor	1	3.57	54	54
Rhabdoid Tumor	1	3.57	32	32
Synovial Sarcoma	1	3.57	59	59
CD99+ Malignant Neoplasm	1	3.57	72	72
Undifferentiated Sarcoma	1	3.57	106	106
Total	28	100	54.57 ± 22.16	32 - 109

Table 3. Overall Turnaround Time and at Specific Time Points

Time Point	N	Mean TAT ± SD (days)	Range
Pre-analytical:	232	1.89 ± 0.59	0 – 8
Accession time to grossing time	232	0.51 ± 0.51	0 – 2
Grossing time to availability of H&E slides	232	1.38 ± 0.67	1 – 3
Analytical:	232	11.56 ± 3.39	0 – 82
Availability of H&E slides to initial review with consultant pathologist	232	1.98 ± 1.63	0 – 6
Initial review of slides with consultant pathologist to release of initial histopathology report	232	9.58 ± 5.15	2 – 29
Request for immunohistochemical stains to charging of stains	141	3.10 ± 3.25	0 – 15
Post-analytical: Initial review of the supplementary slides to release of supplementary/ final histopathology report	70	4.53 ± 4.90	0 – 20
Overall	232	13.39 ± 6.30	2 – 32

Table 4. Multivariate Analysis, and p-values of the Tested Factors

	Multivariate		
	Beta	SE	p value
Additional processing			
Performed	-0.71	1.24	0.5647
Not performed	Reference		
Regrossing			
Performed	-0.56	1.54	0.7186
Not performed	Reference		
Immunohistochemical			
Performed outside	6.4	1.14	<0.0001*
Performed in-house/not applicable	Reference		
COVID-19 pandemic [Yes]			
Yes	-2.42	0.78	0.0021*
No	Reference		

*significant

days (SD ± 6.30, range 2-32 days). Rhabdoid tumors had the longest TAT (mean: 23 days), followed by CIC-rearranged sarcoma and desmoplastic small round cell tumors. Pleuropulmonary blastoma and Wilms tumor had the shortest TATs, with means of 4 and 9.16 days, respectively (Table 1). Cases without IHC stains had a mean TAT of 9.45 days (SD ± 4.09, range 2-23 days), compared to 15.86 days (SD ± 6.20, range 4-32 days) for those requiring IHC.

The mean TAT, when analyzed by phase revealed the following: pre-analytical phase: 1.89 days (SD ± 0.59); analytical phase: 11.56 days (SD ± 3.39); post-analytical phase: 4.53 days (SD ± 4.90). The charging of IHC stains from the time it was requested took an average of 3.10 days (Table 3).

Several factors were analyzed for their impact on TAT (Table 4). IHC stains performed outside the institution significantly prolonged TAT (mean: 19.53 days, p = <0.0001). Additional processing (p = 0.5647) and specimen regrossing (p = 0.7186) did not significantly affect TAT. A shorter overall TAT (11.89 days, p = 0.0021) was observed during the COVID-19 pandemic. The same held true when analyzing only the subset of cases during the same period that had IHC stains performed (TAT: 13.44 days, p = <0.0001). On average, about 3 consultant pathologists (SD ± 1.96, range 1-12 consultants) were onboard a case. A positive correlation (rs = 0.27, p < 0.0001) was found between the number of consultant pathologists reviewing a case and the mean TAT. Thirteen cases were referred for external consultation, with rhabdomyosarcoma accounting for the largest proportion (n = 4, 30.77%). The mean turnaround time (TAT) for cases with external consultations was 18.54 days (SD ± 7.65).

Challenging cases with unclear diagnoses or incomplete work-up of the 232 cases, 28 (12.07%) did not yield a definitive diagnosis. The main reasons were the unavailability of molecular tests (61%, n = 17), lack of IHC stains (21%, n = 6), and insufficient tissue for further analysis (18%, n = 5). None of the cases had insufficient clinical or radiological information.

Discussion

Cancer in the pediatric age group is less common than in adults, accounting for only 1-5% of all malignancies. However, approximately 400,000 children are diagnosed globally each year [10]. The Philippine Children's Medical Center (PCMC), the largest pediatric hospital and a referral center for complex pediatric care in the country, had 36% of its 4,924 admissions in 2021 related to cancer [12]. Among these, PSRBCTs were notably prevalent.

Male predominance in childhood cancer has been documented, with a male-to-female ratio of 1.19 in one large study [13], similar to the current cohort's ratio of 1.04. In Southeast Asia, the most common PSRBCTs are retinoblastoma, non-Hodgkin lymphoma, and Wilms tumor [14]. Similarly in this study, the most frequently encountered tumors in order of prevalence were Wilms tumor, retinoblastoma, neuroblastoma, and lymphoblastic lymphoma.

Maintaining an ideal turnaround time (TAT) is crucial for prompt diagnosis, reducing morbidity and mortality by enabling timely and appropriate treatment, ultimately improving outcomes [4]. In the 1990s, the College of American Pathologists recommended finalizing reports within two working days for routine cases. The

Association of Directors of Anatomic and Surgical Pathology (ADASP) suggested that 80% of routine biopsies be completed within two working days or have a written report within three working days [7]. However, no specific guidelines were provided for large or complex cases [15]. The ADASP's 2006 revision recommended including TAT as a component of quality assurance and improvement plans for various specimens, but no international standards for histopathology TAT have been established [7].

This study found a mean TAT of approximately 13 calendar days for diagnosing PSRBCTs. International studies report mean TATs of 3 to 7.5 days for general surgical cases [4, 16, 17], while studies from developing countries report a median TAT of about a month. For large or complex specimens, a study found a median TAT of 4 days, which increased for radical cancer resections and other malignant cases [7]. A local study conducted near Manila, the capital of the Philippines, reported a mean TAT of 5 days for complex resection specimens and malignant cases [8]. In contrast, Boston Children's Hospital, which processes 12,000 to 13,000 pediatric specimens annually, had a mean TAT of 3.1 days for surgical pathology cases during the study period (unpublished data).

Consider highlighting tumors with the shortest TAT, such as pleuropulmonary blastoma (PPB) and Wilms tumor. These organ-specific tumors can often be diagnosed based on morphology alone, reducing the need for additional studies and expediting the diagnostic process. However, nuances exist (molecular studies to confirm DICER1 variant in PPB and WT1 IHC particularly for Wilms tumor cases showing atypical features). In this study, the longest TAT was for rhabdoid tumor, CIC-rearranged sarcoma, and desmoplastic small round cell tumor (DSRCT). Rhabdoid tumor can often be excluded with a single immunostain (INI-1), typically ordered early in the workup in North American practice when the morphology is suspicious. CIC-rearranged sarcoma and DSRCT are more challenging, both requiring molecular confirmation, demonstration of a C-terminus WT-1 immunoreactivity using an immunostain that is not locally available for the latter, and often a complex exclusionary diagnostic process for CIC-rearranged sarcoma. Similar to the utility of INI-1 in diagnosing rhabdoid tumors, other immunostains, such as PHOX2B for neuroblastoma and NKX2.2 for Ewing sarcoma, are valuable for confirming a diagnosis when correlated with the appropriate clinical and morphologic features. Thus, pediatric centers diagnosing childhood malignancies should ensure that these immunostains are available in-house.

Given the rarity of some PSRBCTs, acquiring reagents and testing platforms for these infrequent tumor cases can be financially challenging. A more practical approach may involve focusing on more commonly encountered pediatric tumors, based on the institution's experience and regional statistics, and building diagnostic armamentarium around these cancer types. Many U.S. children's hospitals design their own menu of immunohistochemical stains and molecular testing platforms tailored to the pediatric population they serve.

In this study, the pre-analytical phase generally took about one day per step. At PCMC, a daily 3 p.m. cut-off time for grossing is implemented, and slide processing occurs only from Sunday to Thursday. Despite these parameters, the general TAT remains unaffected. Slides are typically available in the afternoon, and on average, it takes about two days for the first consultant to review the case after the slides are released. This interval is mainly due to the resident pathologist needing more time to study the case before presenting it to the consultant. From the time the consultant sees the case to the release of the initial report, the average TAT was 10 days, the longest segment in this study. Supplementary reports (issued for 70 cases, comprising 30% of the total analyzed), often requested due to additional IHC or special stains (some of which are performed in another laboratory) had an average TAT of 5 days (range: 0-20 days), indicating that cases can be finalized more quickly when these stains are readily accessible.

When grouping these time points into pre-, analytical, and post-analytical phases, the analytical phase had the longest TAT. This contrasts with another study that found the pre-analytical phase (from transport to slide processing) to have the longest TAT, in a resource-poor area [5].

For in-house IHC, the TAT was generally 3 days, calculated from the time IHCs were requested to when the stains were completed and charged. In PCMC, IHCs can be billed immediately if the patient is still admitted, reducing the TAT. For discharged or outpatient cases, contacting relatives for payment processing is the biggest hurdle, potentially prolonging the TAT. While this is uncommon for routine IHCs in other countries, it highlights the challenges posed by the "out-of-pocket payment system", which is common in developing countries with similar healthcare models. A US-based study also noted that IHCs can prolong TAT [15]. However, IHCs are crucial especially in regions with limited access to molecular testing, as they often serve as surrogate tests to provide a more accurate diagnosis. Sending slides to an outside laboratory for IHC stains that are unavailable in-house significantly prolongs the TAT, with processing typically taking an additional week. Financial barriers also affect the timeline, as relatives are required to pay part of the processing fee. Additional processing steps, such as extended fixation time, decalcification, or additional sections, did not significantly impact TAT in this study. This finding contrasts with one study where decalcification delayed TAT [17] but aligns with another study where it was not a significant factor [15].

The COVID-19 pandemic restricted hospital operations globally. It was hypothesized to negatively affect TAT due to reduced staff availability and unfamiliar workflows for patients. However, this study found that the pandemic actually shortened the overall TAT including the TAT for IHC performed at another institution. The increased use of telepathology improved the efficiency of external expert reviews, leading to faster TATs, as highlighted in one study [6]. Online communication platforms, more widely used during the pandemic, facilitated case discussions and allowed local and international

subspecialists to participate. Additionally, the suspension of many elective procedures reduced the volume of specimens processed, while online payment transactions streamlined patient payments, further enhancing TAT. The pandemic highlighted the value of telepathology and other streamlining processes introduced during that period in improving workflow efficiency; consequently, these practices have been integrated into hospital operations beyond the pandemic.

Intradepartmental consultations are common, especially for complex cases, as pathologists often have areas of specialization. Some cases require expert consultations from pathologists in other institutions, including international ones. These consultations are typically conducted by sending histology slides or through telepathology. Telepathology facilitates quicker and more accurate diagnoses, which significantly impacts treatment plans and prognoses [5, 6]. The mean TAT of 18 days for external consultations was observed to be longer than the overall mean TAT of 13 days, which might be explained by the fact that these consult cases most likely have been passed around first intradepartmentally before being referred to the non-affiliated experts. A Swiss Sarcoma Network study highlighted diagnoses rendered by general pathologists that often took longer than those rendered by subspecialty-trained pathologists, emphasizing the importance of subspecialty training in improving diagnostic efficiency [18].

This study found that the greater the number of pathologists consulted, the longer the TAT, which was expected. Multiple consultations often indicate a challenging case or a lack of expertise in handling such cases. The latter is a known issue in developing countries, as noted in a recent pediatric pathology workshop in Indonesia [19]. At the time of writing,, there are 25 in-house pathologists that sign out pediatric cases at PCMC, with two (8%) consultants having received a formal training in pediatric pathology in another country. This gap can be addressed by investing in subspecialty training for local pathologists, supporting regional and national expert-led conferences and workshops, and holding regular consensus conferences within the department. Studies from Nigeria and the United States similarly identified intradepartmental consultations as a reason for prolonged TAT [15-16]. Studies in other countries have shown discordance rates of 9% to 29% between diagnoses by general pathologists and specialists, highlighting the value of subspecialty-trained experts [19-23].

Rendering a definitive diagnosis can sometimes be challenging due to sampling issues, as observed in 5 cases in our cohort. Sampling issues are a well-recognized factor contributing to diagnostic delays [24]. Providing regular feedback to surgeons and interventional radiologists on specimen adequacy would help address this as certain tumors may require specific techniques (e.g., open biopsy vs. core needle biopsy for bony lesions) for accurate diagnosis [25].

The lack of access to advanced ancillary tests, such as molecular testing and specific IHC stains, is a major barrier to confirm diagnoses. These tests not only assist in tumor classification but also provide critical information for treatment and prognosis [11]. Expanding access to key ancillary tests, starting with relevant immunohistochemical stains, will enhance diagnostic capability and foster local expertise, as demonstrated in a pathology capacity-building project by Santiago and colleagues [26, 27]. Additionally, molecular test is necessary to exclude the presence of germline mutations in certain tumors (e.g. DICER1 tumor predisposition syndrome), which could have implications for living family members [28].

Importantly, none of the cases lacked clinical information, which has been identified as a delay factor in other studies [16, 29], indicating good communication between pathologists and clinicians.

Conclusions and Future Directions

In summary, this study identified key factors affecting TAT for PSRBCT histopathology reports at the Philippines' largest pediatric hospital. These factors include limited access to certain IHC stains in-house, the need for multiple pathologists' consultations, and the unavailability of molecular tests. Improvement efforts should focus on these areas, such as making key immunostains for common pediatric tumors available in-house and increasing the number of formally trained pediatric pathologists.

The study could be expanded longitudinally to track progress as the laboratory acquires new IHC stains and molecular tests. Regular analysis of TAT as a quality assurance tool could help identify areas needing attention. Further research on how TAT impacts treatment initiation and patient outcomes in PSRBCTs would provide valuable insights.

Author Contribution Statement

GA: project administration, data collection, formal analysis, and interpretation, drafting of the manuscript; CM: project administration, review and editing of the manuscript; MHS, RWL, CI, and JP: review and editing of the manuscript; CKC: conceived and directed the study, data interpretation, drafting, review, and editing of the manuscript.

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General

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Approval

This research has been approved by Clinical Research Department and the Institutional Research – Ethics Committee of the Philippine Children's Medical Center (PCMC IR-EC 2023-026, approval date: May 24, 2023).

Ethical Declaration

This research strictly complied with the Philippine Data Privacy Act of 2012 and National Ethical Guidelines for Health and Health-Related Research of 2017.

Study Registration

The study has not been registered in any registration dataset.

Conflict of Interest

All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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