The Profile of Thrombocytosis in Pediatric Intensive Care Unit

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Objective: To describe the distribution of thrombocytosis in pediatric intensive care unit.
Methods: A retrospective study reviewed medical chart of all children in Pediatric Intensive Care Unit (PICU) Haji Adam Malik Hospital with all diagnosis during January 2007 – December 2007. All the patients who diagnosed as thrombocytosis were enrolled to this study. The data was collected include age, sex, diagnosis in PICU will be reported descriptively.
Results: From the total 319 cases admitted to PICU, there were 65 had thrombocytosis. Most thrombocytosis 29(65) were in group age 1-5 years, and 21(65) in group 5-10 years, and 15(65) in group age more than 10 years. Boys more than girls (35 vs 30). Thrombocytosis occurred mostly in complicated surgical patients, head injury and infectious diseases. Conclusion: Thrombocytosis is common problem in critically ill patient. It is required a longitudinal study to determine the cause of thrombocytosis in critically ill patients.
Keywords: thrombocytosis, critically ill patients, PICU

Abstrak: Latar belakang: Pada pasien yang dirawat di PICU trombositosis biasa terjadi secara sekunder atau merupakan reaksi terhadap beberapa factor penyebab. Trombositosis reaktif biasanya disebabkan peningkatan pelepasan sejumlah sitokin sebagai respon terhadap infeksi, inflamasi, vaskulitis, trauma jaringan, dan factor-faktor penyebab lain. Tidak ada bukti yang menyatakan bahwa kejadian berbeda secara signifikan antara satu negara, ataupun antar etnik yang berbeda maupun akipat perbedaan letak seperti geografis Indonesia sebagai negara kepulauan.
Tujuan: Menggambarkan kejadian trombositosis pada pasien sakit berat yang dirawat di PICU.
Kesimpulan: Trombositosis merupakan masalah yang sering terjadi pada pasien yang sakit berat seperti pasien – pasien yang memerlukan perawatan di PICU. Perlu dilakukan penelitian lebih lanjut untuk menjelaskan penyebab trombositosis pada pasien sakit berat.
Kata kunci: trombositosis, pasien sakit berat, PICU
INTRODUCTION

Thrombocytosis is classified as either primary or secondary. Thrombocytosis in infancy and childhood is not an uncommon condition. There are very few local paediatric literature on its incidence and clinical significance. This is probably because platelet count involves tedious manual counting.\(^{1,4}\) Furthermore, primary thrombocytosis is extremely rare in childhood. It is usually secondary to other underlying conditions. The physiologic reference range of platelet counts is 150-400 \(\times 10^9/L\). A platelet count exceeding the upper limit is called thrombocytosis. Primary thrombocytosis is caused by autonomous production of platelets unregulated by the physiologic feedback mechanism to keep the count within the reference range. Primary thrombocytosis is a component of a myeloproliferative disorder (eg, essential thrombocythemia, myelofibrosis with myeloid metaplasia, polycythemia vera, chronic myelocytic leukemia [rare]) or, in rare cases, of acute myelocytic leukemia.\(^{5,7}\) In contrast to primary thrombocytosis, secondary thrombocytosis is an exaggerated physiologic response to a primary problem, such as an infection. In pediatrics, primary thrombocytosis is exceedingly rare, whereas secondary, or reactive, thrombocytosis is common, particularly in infants. Secondary thrombocytosis (the term reactive thrombocytosis is used in all subsequent discussions) usually is transient and subsides when the primary stimulus ceases. In spite of the strikingly high platelet count thrombotic and/or hemorrhagic complications are highly exceptional.\(^{8,12}\) This is in contrast to thrombosis and bleeding that develop more commonly as complications of primary thrombocythemia. Dame and Sutor stated that the annual incidence of newly diagnosed primary thrombocytosis in childhood is 1 case per 10 million population. According to these authors, about 75 children with primary thrombocytosis were reported from 1966-2000.\(^{3,5}\) Dror et al published the results of an analysis of 36 children with essential thrombocytosis. The frequency of reactive thrombocytosis is far more common than essential thrombocytosis and depends on age. Rates are highest during the first 3 months of life. Preterm infants have higher frequencies than those of term infants.\(^{13}\) According to Sutor’s summarization of the findings from several studies, 3-13\% of hospitalized pediatric patients had a thromboocyte count of more than 500 \(\times 10^9/L\). In one study, 0.5\% of hospitalized children had a platelet count more than 800 \(\times 10^9/L\). No evidence suggests that the incidences of either primary or reactive thrombocytosis vary significantly from one country to another or from one ethnic group to another. In patients with primary thrombocytosis, which is a myeloproliferative disorder, the frequency of thrombosis and/or hemorrhage widely varies among various reports (20-84\% for thrombotic complications and 4-41\% for bleeding complications).\(^{2,5}\) However, these statistics are for adult patients, and incidences of hemorrhagic and thrombotic complications in primary thrombocytosis of children are not known.\(^{1,6}\) There is only limited study reported thrombocytosis in the Pediatric Intensive Care Unit (PICU) patients. This study objective is to describe the profile of thrombocytosis in PICU in Haji Adam Malik Hospital Medan.

METHODS

A retrospective study reviewed medical chart of all children in Pediatric Intensive Care Unit (PICU) Haji Adam Malik Hospital with all diagnosis during January 2007 – December 2007. All the patients who diagnosed as thrombocytosis were enrolled to this study. The data was collected include age, sex, diagnosis in PICU will be reported descriptively.

RESULTS

During our study period there were 329 patients in PICU with all causes that hospitalized in PICU. From 329 cases, there were 204 had normal platelet, and 65 patients had thrombocytosis and 60 patients had thrombocytopenia.
Table 1.

Distribution of platelet status in PICU patients

<table>
<thead>
<tr>
<th>Platelet status</th>
<th>N=329</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia</td>
<td>60</td>
</tr>
<tr>
<td>Normal</td>
<td>204</td>
</tr>
<tr>
<td>Thrombocytosis</td>
<td>65</td>
</tr>
</tbody>
</table>

Table 2 showed that thrombocytosis occurred most in group age 1 – 5 years, followed by group age 5 – 10 years and > 10 years in 29 cases, 21 cases and 15 cases consecutively. There were 35 boys had thrombocytosis compared to 30 cases in girls.

Table 2.

Distribution of thrombocytosis based on age and sex

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>N=65</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-5</td>
<td>29</td>
</tr>
<tr>
<td>5-10</td>
<td>21</td>
</tr>
<tr>
<td>&gt;10</td>
<td>15</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sex</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Boys</td>
<td>35</td>
</tr>
<tr>
<td>Girls</td>
<td>30</td>
</tr>
</tbody>
</table>

Table 3.

Underlying diseases in thrombocytosis

<table>
<thead>
<tr>
<th>N=65</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complicated surgery</td>
</tr>
<tr>
<td>Infectious diseases</td>
</tr>
<tr>
<td>Head injury</td>
</tr>
<tr>
<td>Others</td>
</tr>
</tbody>
</table>

The underlying disease of thrombocytosis in this study were complicated surgery in 31 cases, infectious diseases in 21 cases, head injury in 10 cases and others in 3 cases.

DISCUSSION

Denton et al, reported that extreme thrombocytosis (ExtThr; platelet count $\geq 1000 \times 10^9/\text{l}$) is uncommon but may have an increased occurrence in critically ill children. The incidence of ExtThr for children on the Paediatric Intensive Care Unit at Bristol Royal Hospital for Children between January 2001 and December 2004 was calculated, and the notes of children identified with ExtThr were reviewed for possible common aetiological factors, potential treatment regimes and outcome. Vorat et al estimated the incidence and causes of secondary thrombocytosis in children, a 12 month study of all patients attending a children’s hospital and discovered to have a platelet count over two times the upper normal limit (> 800 x 10(9)/l) was undertaken. Data so obtained were analysed both separately and together with those from two previous studies to gain as broad a perspective as possible. Of 7916 children who had platelet counts during the study period, 36 (0.5%) produced a value > 800 x 10(9)/l; there were 19 boys and 17 girls. There was a preponderance of young infants (median age 13 months). Twenty seven of the 36 had some sort of associated infection, bacterial in 18 and viral in nine. The other nine were either recovering from anti-neoplastic chemotherapy (n = 6), were post-operative (n = 2), or simply iron deficient (n = 1). Combining these patients with those described in previous studies allowed a review of 139 unselected children with very high platelet counts. Fifty three (38%) had infections, 29 (20%) had traumatic or surgical tissue damage, 16 (11%) had malignant disease undergoing chemotherapy or surgery, and 13 (9%) had connective tissue or autoimmune disorders. Secondary thrombocytosis is not rare and is most frequently seen in very young infants after infection. It can arise in a wide variety of other circumstances including rebound from myelosuppression, iron lack, or as part of an acute phase response. It is clinically unimportant in terms of morbidity and requires no treatment other than that for the primary condition. Yohannan et al, study in six hundred sixty-three children aged 1 to 16 years with thrombocytosis (defined as a platelet count of more than 500 X 10(9)/L) seen in a university hospital over a 1-year period were studied prospectively for etiology. The causes of thrombocytosis were infection (30.6%), hemolytic anemia(19.3%), tissue damage (15.2%), rebound thrombocytosis (14.8%), chronic inflammation (4.1 %), renal
disorders (4.1 %), and malignancy (2%). Thrombocytosis associated with multiple, simultaneous causative factors was seen in 3.3% of cases. Among all patients with infections, osteomyelitis and septic arthritis were associated with higher platelet counts than other infections ($P<0.0001$).

Thrombocytosis secondary to infections was significantly more common in children under 5 years of age, whereas chronic inflammation, malignancy, and renal disorders were more common causes of thrombocytosis in children over 5 years of age. Thrombocytosis of 1 million or more platelets was seen in 13 (2%) children. No thrombocytosis-related complications were seen in any children, and none required any specific treatment. Thrombocytosis is a frequent finding in children. It is due to a variety of etiologic factors and is of little clinical discriminatory value. It is often due to an acute-phase phenomenon in response to infection, tissue damage, blood loss, or anemia, and is rarely due to malignancy. Vannucchi et al, studied about the role of elevated platelet counts in thrombosis, which represent the predominant complication of CMPD, significantly affecting prognosis and quality of life as well as, paradoxically, in the pathogenesis of the hemorrhagic manifestations, will be discussed. Established and novel potential risk factors for thrombosis, including the clinical relevance of the JAK2V617F mutation, and current management strategies for thrombocytosis are also briefly discussed. Shafer et al, noted in his study that the challenge of correctly identifying the cause of thrombocytosis in an individual patient becomes particularly critical when the clinician is confronted with treatment decisions. Patients with secondary (reactive) thrombocytosis do not require platelet-lowering or antiplatelet treatment because their abnormal platelet count itself does not place them at risk for hemostatic or vascular events. It is crucial, however, to identify the cause of their secondary thrombocytosis, even when it is clinically inapparent, so that treatment can be directed to the underlying disease. A normal erythrocyte sedimentation rate and a normal level of C-reactive protein may help to rule out an underlying inflammatory disorder. The search for occult cancer should involve a thorough physical examination, including examination of stool specimens for occult blood, chest radiography, and further testing as indicated by systemic and localizing symptoms and signs.

Chan et al, reported the introduction of the newer generation of electronic cell counters allows the routine reporting of platelet numbers when the peripheral blood count is requested. In a 12-month period, 100 episodes of marked thrombocytosis (platelet count more than 900 x 10^9/L) were found among 94 children. These patients were young (median age 9 months). All but one episode of marked thrombocytosis occurred as a phenomenon secondary to a variety of disease states. Infections, especially those involving the central nervous systems were the commonest cause of an elevated platelet count in this series. Malignant diseases alone were rarely associated with thrombocytosis of this magnitude. The elevated platelet count began to decline at a mean of 3 days after diagnosis, and no thrombotic or hemorrhagic complications were encountered. Marked thrombocytosis is a benign, common phenomenon in young children, but specific treatment is not required. Natalie et al, on their study objecyive to estimate the frequency of primary and secondary thrombocytosis in children. To describe the diseases associated with secondary thrombocytosis. To relate the magnitude of the thrombocytosis and the different diagnoses. Resulted that 584 cases of thrombocytosis were found and their study, representing 32.4% of the blood counts. 334 clinical case notes were reviewed, 62% male. 3 patients 0.9% had a platelet count over 1,000,000, 2 of them had primary thrombocytosis (essential thrombocythaemia and chronic myeloid leukaemia) and the third had a bacterial meningitis. The diseases associated with secondary thrombocytosis were infection 48.8% (respiratory 70%), iron deficiency 18.6% tissue damage (burns and surgery) 12.6%. Concluded that the frequency of primary thrombocytosis is low, when it is less than 1,000,000 a secondary aetiology is most likely. Heng et al, reported that primary thrombocytosis is extremely rare in childhood. It is usually an acute phase reactant secondary to other inflammatory
process. The mechanism by which the acute
inflammation causes thrombocytosis is not
fully understood. Two humoral factors,
thrombopoietin and megakaryocyte colony
stimulating factor appear to regulate the
production and the numbers of circulating
platelets. There is a wide variety of causes
associated with thrombocytosis. In our study,
bacterial infection in particular pneumonia
was the predominant cause of thrombocytosis.
Other common conditions included urinary
tract infection, gastroenteritis and Kawasaki’s
disease. Secondary thrombocytosis is a benign
and self-limiting condition. None of the cases
developed any complications associated with
the high platelet level. This could have
accounted for the low proportion of followed-
up platelet count especially when the child
had recovered from the underlying illness.
The onset of thrombocytosis occurred within
the first week of illness in majority of the
illness. The normalisation time depends on
the severity of inflammation. Generally, the
normalisation time is longer in bacterial
infections compared to the viral infections.

Kousaku et al, determine the incidence and
etiology of childhood thrombocytosis, over 15,000 platelet counts in 7,539 patients
performed at a single regional hospital were
reviewed. When thrombocytosis was defined
as ≥500 x 10^9/l of platelet counts, the
condition could be diagnosed in 6.0% (456
cases) of the patients. All patients were
classified as having secondary thrombocytosis.
The incidence of thrombocytosis dramatically
changed throughout child development; it was
12.5% in neonates, peaked to 35.8% in 1-
month-old infants and then returned to 12.9%
in 6- to 11-month-old infants. Thereafter, it
gradually decreased with age to only 0.6% in 11-
to 15-year-old children. Frequent causes of
thrombocytosis included infection (67.5%),
Kawasaki disease (9.4%), prematurity (7.7%) and
iron deficiency anemia (6.4%). Thrombocytosis was an incidental finding in a
substantial population of early infants. Thrombocytosis as a reaction to several types
of infection and Kawasaki disease was more
common in children under 7 years old, while
autoimmune disease and tissue damage were
major causes in children aged 11-15 years. No
child had thromboembolic complications.
These findings indicate that childhood
thrombocytosis is a benign condition and its
incidence and etiology seem to depend on age.
Conclusion: Thrombocytosis is common
problem in critically ill patient. It is required a
longitudinal study to determine the cause of
thrombocytosis in critically ill patients.

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