

Disease Burden of Immune Thrombocytopenic Purpura among Adult Patients: The Analysis of Thailand Healthcare Databases 2010

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Background: Immune thrombocytopenic purpura (ITP) is not rare disease and it is potentially fatal, particularly in patients with bleeding events which usually lead to hospitalization. Current data on the impact and disease burden of ITP in Thailand are lacking.

Objective: To determine admission rate, mortality rate, hospital cost, length of hospital stay, co-morbidities, treatment and major bleeding events in patients with ITP.

Material and Method: The authors analyzed the data of inpatients with a diagnosis of ITP according to ICD 10 coded D69.3 which were retrieved from a nationwide health financing schemes in fiscal 2010. The data were analyzed by age groups, gender and health financing schemes.

Results: The overall admission rate and mortality rate were 7.68 and 0.29 per 100,000 populations, respectively and increased with age. Women were predominant. Average hospital costs and hospital stays were 27,133 Baht and 6.7 days per admission, respectively and slightly higher among men than women. The most common co-morbidity was hypertension. Gastrointestinal hemorrhage was the most common bleeding event which was 21.5 per 1,000 admissions. Patients in the civil servant medical benefit scheme had the highest percentage of high cost treatment accessibility.

Conclusion: The admission rate, mortality rate and major bleeding events increased with age and was higher among women than men. Average hospital cost and length of hospital stay are higher in men than women. Common co-morbidities may be related to the treatment of ITP. There are the differences in high-cost treatment accessibility between health insurance schemes.

Keywords: Idiopathic thrombocytopenic purpura, Burden of disease, Population-based study

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Immune thrombocytopenic purpura (ITP) is a disease caused by immune-mediated platelet destruction and the decrease of platelet production resulting in low platelet count. Previous studies have showed that persistently low platelet count in patients with ITP was associated with high risk of death from bleeding events, especially in older adults^(1,2). Previous epidemiological studies in adult patients with ITP have found the incidence varied from 1.6 to 3.9 per 100,000 person-year (PYs)⁽³⁻⁵⁾ and the prevalence ranged from 9.5 to 80 per 100,000 persons⁽⁶⁻⁸⁾. The diversity of incidence and prevalence in individuals study based on the limitations of data and exclusion criteria varied

between studies. Although the incidence of ITP was low, the disease can be fatal, particularly in patients with an adverse hemorrhagic complications leading to hospitalization. A recent study on the disease burden of ITP in the United States found that ITP-related hospitalization was associated with longer average length of hospital stay, a higher hospital charge and a higher in-hospital mortality rate when compared to other hospitalized patients⁽⁹⁾.

Moreover, previous population-based studies have demonstrated the association of various co-morbidities in patients with ITP for instance, cataracts, Hodgkin lymphoma, diabetes mellitus, renal failure, vascular event, leukemia, hypertension, anemia and hyperlipidemia⁽¹⁰⁻¹⁴⁾.

Thus, it is important to determine the disease burden to understand the impact of ITP on morbidity and mortality rate and the burden of ITP on medical

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resource utilization. However, at present the published data about the disease burden in ITP are limited. Furthermore, the studies of the impact and the disease burden of ITP in Thailand are still lacking. The authors therefore aim to study the impact and the disease burden of ITP in Thailand.

Objective

The primary objective was to determine admission rate, mortality rate, length of hospital stay and hospital charge. The secondary objective was to identify the common coexistence medical conditions in patients with ITP, to determine the accessibility to high cost treatment in different health care schemes and to find the rate of major bleeding events.

Material and Method

Patient population

This was a cross-sectional study. Data included inpatient Medical Expensing Forms for the fiscal year 2010 (October 1, 2009 and September 30, 2010) from nationwide Thailand healthcare databases including 1) the National Health Security Office (NHSO), 2) the Civil Servants Benefit System from the Comptroller General's Department and 3) the Social Security Office. Data received by the analyst team was checked for accuracy by looking for (a) overlapping information (b) visit dates (c) missing items (d) incorrect coding and (e) dating with the correct fiscal year.

Patients were classified into 7 age groups as follow: 18-30, 31-40, 41-50, 51-60, 61-70, 71-80 and > 80 years.

The diagnosis of idiopathic thrombocytopenic purpura

The diagnosis of ITP was based on ICD-10 code D69.3 from both primary diagnosis and secondary diagnosis. The authors excluded patients with medical condition that might caused thrombocytopenia including: HIV (B20-B24), Hematologic malignancy (C81-C96), liver disease (K70-K77), systemic lupus erythematosus (M32), thrombotic thrombocytopenic purpura (M31.1), disseminated intravascular coagulation (D65), secondary thrombocytopenia included drug-induced thrombocytopenia, dilutional thrombocytopenia (D69.5).

Treatment

The treatment was identified by ICD 9-CM code including injection and infusion of gamma globulin (99.14), splenectomy (41.5, 41.43), transfusion of

coagulation factor (99.06). We analyzed the treatment accessibility by patient's health care insurance.

Major bleeding events

Major bleeding events were identified in ITP patients by the coexistence of ICD 10 codes as follow: intracerebral/intracranial hemorrhage (I61, I62), gastrointestinal hemorrhage (K92), hemoptysis (R04.2) and hematuria (R31).

Outcome measures

The present study outcomes were admission rate and mortality rate per 100,000 populations in the same age groups; 18-30, 31-40, 41-50, 51-60, 61-70, 71-80 and over 80 years. The length of hospital stay and health care costs were reported in days and baht per admission. The comorbidities were ranked from the top ten medical conditions. The treatment accessibility was reported as percentages of admission. The rate of major bleeding events was calculated per 1,000 admissions.

Statistical analysis

The variables and interrelationships were analyzed using the SPSS program and verified before analyzing. After analyzing the data, the research team passed the primary analysis to ten medical specialists in order to check the validity of the information. Upon confirmation of validity, the data were compared to the Ministry of Public Health's Statistics Report 2010 for trend congruence as well as the hospital's mortality reporting for each age and disease group for comparison with the national Death Registration of the Registry Administration, Ministry of Interior Affairs⁽¹⁵⁾. Ethics approval was provided by Ethic Committee of Medicine Faculty, Khon Kaen University under the respect of Helsinki Declaration.

Results

Admission rate and mortality rate

The total admissions were 3,627 times per year. The overall ITP admission rates were 7.68 per 100,000 populations in the same age group and were significantly higher in women than men [10.4 (95% CI; 10.01-10.83) vs. 4.78 (95% CI; 4.51-5.08) per 100,000 populations]. The admission rates increased with age and were higher among women than men in all age groups, except for those patients older than 80 years old as shown in Fig 1. The total in-hospital death were 137 persons per year. The overall mortality rates were 0.29 per 100,000 populations. The mortality rates were

higher in women than men with an estimated ratio of 2:1 [0.37 (95% CI; 0.298-0.455) vs. 0.206 (95% CI; 0.151 – 0.273) per 100,000 persons] which significantly increased with age as shown in Fig 2.

Hospital cost and length of hospital stay

The total hospital charges of ITP were 98,413,523 baht per year and mean \pm SD of hospital cost was 27,133 \pm 74,005 Baht per admission. The hospital cost was higher in men than women (29,922 Baht vs. 25,929 Baht). The total length of hospital stay was 23,478 days per year and mean \pm SD of length of hospital stay was 6.47 \pm 10.89 days which was slightly higher in men than women (6.7 days vs. 6.38 days) as shown in Table 1. An average hospital charge was different among health financing schemes. The patients in the civil servant group have the highest mean of hospital cost and patients in universal health insurance coverage group have the lowest average hospital cost as shown in Table 2.

Co-morbidities

The top ten most common coexistence medical conditions in adult patients with ITP were; hypertension, diabetes mellitus, anemia, hyperlipidemia, urinary tract infection, sepsis, chronic kidney disease, acute respiratory failure and gastroenteritis respectively as shown in Table 3.

Treatment

A. Splenectomy: the percentage of patients who underwent splenectomy was highest among

patients in social health insurance and lowest in civil servant medical benefit scheme.

B. Intravenous immunoglobulin: the

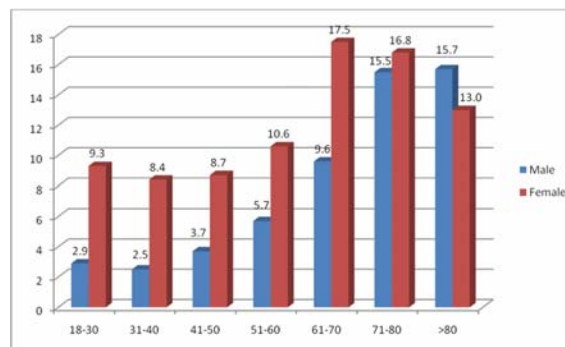


Fig. 1 Admission rates of ITP per 100,000 populations by age group in 2010

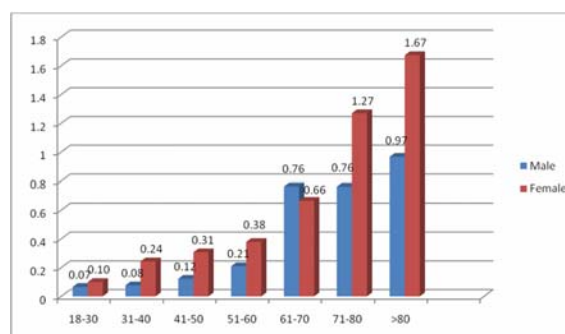


Fig. 2 Mortality rates of ITP per 100,000 populations by age group in 2010

Table 1. Hospital cost and length of hospital stay per admission in ITP patients in 2010

Variables	Women	Men
Hospital cost (Baht)		
Sum	65,678,437	32,735,086
Mean \pm SD	25,929.11 \pm 74,145.54	29,922.38 \pm 73,637.33
Length of hospital stay (day)		
Sum	16,151	7,327
Mean \pm SD	6.38 \pm 11.94	6.7 \pm 7.94

Table 2. Hospital cost per admission in adult patients with ITP by health care financing schemes in 2010

Variables	Civil servant benefit	Social health insurance	Universal coverage
Hospital cost (Baht)			
Mean \pm SD	50,394 \pm 135,552	32,731 \pm 69,377	21,592 \pm 55,557
Median (Min-Max)	13,668 (665-1,929,463)	13,975 (690-711,137)	7,515 (50-1,029,016)

percentage of patients receiving intravenous immunoglobulin was highest among patients in civil servant medical benefit scheme and lowest in patients in social health insurance.

C. Transfusion of coagulation factor: the percentage of patients receiving coagulation factor was highest among patients in civil servant medical benefit scheme group and none of patients in social health insurance received this treatment.

Summary of percentage of treatment accessibility by health financing schemes in 2010 are shown in Fig. 3.

Major bleeding events

The rate of major bleeding events in patients with ITP were as follows; gastrointestinal hemorrhage was 21.5 per 1,000 admission, intracerebral/intracranial hemorrhage was 7.7 per 1,000 admissions, hematuria was 5.2 per 1,000 admissions and hemoptysis was 3 per 1,000 admissions, respectively. The rates of major bleeding events increased with age as shown in Fig. 4.

Discussion

The admission rates were relatively low as prevalence cannot be evaluated in the present study due to the limitation of the database, however, the overall admission rates is lower than previous published prevalence. The overall mortality rate is low. As expected, the admission rate and mortality rates increase with age and women are predominant in all age groups. Our results are comparable to previous studies showing that the prevalence, incidence and mortality rate increases with age and is higher among women than men⁽⁵⁻⁸⁾.

The mean hospital cost was found to be lower than previous reports in the United States which may be due to the higher cost of healthcare expenditure.

The average lengths of hospital stay in the present study are equal to the report from Danese M et al namely 6.4 days⁽⁹⁾.

The most common co-morbidities in patients with ITP in our study are similar to previous studies of comorbidities in ITP⁽¹⁰⁻¹⁴⁾ which include hypertension, diabetes mellitus, anemia, acute or chronic renal failure, hyperlipidemia except for autoimmune disease, lymphoma and leukemia because we have excluded

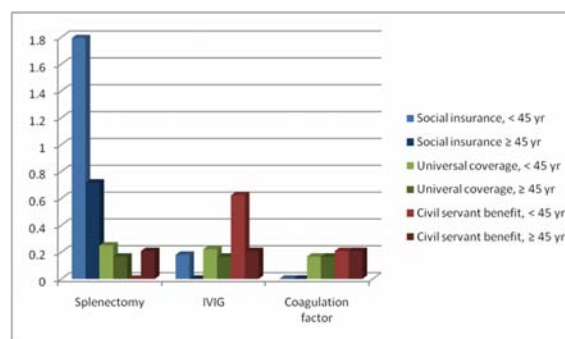


Fig. 3 Percentage of treatment accessibility in ITP by health care financing schemes and age group in 2010

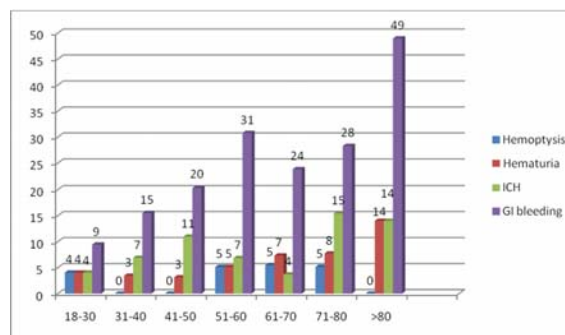


Fig. 4 Rates of major bleeding events in ITP patients per 1,000 admissions by age group in 2010

Table 3. Top ten co-morbidities in adult patients with ITP in 2010

Co-morbidities	Frequency (%)	Rate per 1,000 admissions
1. Essential hypertension	581 (8)	160.18
2. Diabetes Mellitus	197 (2.7)	54.31
3. Anemia	149 (2.06)	41.08
4. Hyperlipidemia	139 (1.92)	38.32
5. Urinary tract infection	104 (1.43)	28.67
6. Sepsis	87 (1.20)	23.98
7. Chronic kidney disease	72 (0.99)	19.85
8. Acute respiratory failure	67 (0.92)	18.47
9. Acute renal failure	64 (0.88)	17.64
10. Gastroenteritis	60 (0.82)	16.54

these conditions before capturing data. Cataract was also not common in the present study which could be due to under diagnosed or investigation. A previous study showed that these coexistence medical conditions can occur before or after diagnosis of ITP⁽¹⁾. The medical conditions which occur before ITP may be the predisposing factors in the mechanism of ITP as reported by Feudjo T et al. They found that hematological disease, dermatological conditions, bleeding disorders and constitutional symptoms frequently occur before the diagnosis of ITP⁽¹⁾. The present study did not demonstrate any temporal relationship between these medical conditions and ITP. However, most of co-morbidities are likely to be related to previous treatment of ITP (corticosteroid, immunosuppressive drug) for instance, diabetes mellitus, sepsis, acute respiratory failure, gastroenteritis. To determine the impact of ITP to other medical conditions, a well-designed cohort study is needed to examine temporal relationships and to identify the association of these medical conditions and ITP.

The present study has demonstrated treatment accessibility differences among health financing schemes. Patients in civil servant medical benefit schemes have the highest percentage of accessibility to high-cost treatment including intravenous immunoglobulin and coagulation factor (it may be implied to recombinant factor VIIa which is off-label use). The patients in the civil servant medical benefit scheme have the lowest percentage of splenectomy which may be because it is an invasive procedure and there are other treatment options, including intravenous immunoglobulin. Patients in universal coverage schemes have a modest percentage of all treatment accessibility. Patients in social health insurance have the lowest percentage of accessibility to high-cost treatment including intravenous immunoglobulin and none of admission in this insurance receive coagulation factor because it cannot be reimbursed by the health financing scheme. Furthermore, patients in this group have the highest percentage of splenectomy which may be due to 2 major reasons. Firstly, splenectomy usually perform in younger patients and patients in this group are probably younger than the other groups. Secondly, patients in social health insurance have the limitation of the reimbursement for other treatment options. The rate of major bleeding events were higher among older adults, a finding which is supported by data from Cortelazzo S et al showing that bleeding complications increase with age⁽²⁾.

Limitations

There are some limitations of the present study. Firstly, the data retrieved from inpatient databases were recorded as admission codes and therefore we cannot identify prevalence rates of ITP as only admission rates are known. Secondly, the diagnosis of ITP, co-morbidities and major bleeding events were based on ICD-10 codes, hence there is the potential for misclassification during data collection, for example, from wrong diagnosis or wrong coding. Thirdly, treatments in the present study were based on the ICD-9 CM codes, hence there is the potential for under or over coding. The results of this study need to be interpreted in the context of its limitations.

Conclusion

The admission rate, mortality rate and major bleeding events increase with age. Admission rate and mortality rates are higher in women than men. The average lengths of hospital stay are comparable to a previous study but the average hospital cost was lower and it was higher in men than women. The common co-morbidities may be related to the treatment of ITP. The percentage of high cost treatment accessibility is highest among patients in civil servant medical benefit schemes, modest in universal coverage schemes and lowest in the social health insurance scheme.

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Potential conflicts of interest

None.

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**ภาระของโรคเก็ดเลือดต่ำจากภูมิคุ้มกันในผู้ป่วยผู้ใหญ่: การวิเคราะห์ฐานข้อมูลเบิกค่ารักษา
ในประเทศไทย ปี พ. ศ. 2553**

ณัฐติยา เตียวตระกูล, จิตติมา ศิริจีระชัย, กาญจนา จันทร์สูง, ชินดล วานิชพงษ์พันธ์, สุมิตร สุตรา

ภูมิหลัง: โรคเก็ดเลือดต่ำจากภูมิคุ้มกัน (ไอทีพี) เป็นโรคที่พบได้ไม่ยากและอาจมีความรุนแรงโดยเฉพาะในผู้ป่วยที่มีภาวะ เลือดออกซึ่งมักจะนำไปสู่การนอนโรงพยาบาล ปัจจุบันข้อมูลเรื่องผลกระทบและภาระของโรค ไอทีพีในประเทศไทย ยังขาดแคลน

วัตถุประสงค์: เพื่อทราบอัตราการนอนโรงพยาบาล อัตราการเสียชีวิต ค่ารักษาพยาบาล ระยะเวลาการนอนโรงพยาบาล โรคที่พบร่วมการรักษาและภาวะเลือดออกที่สำคัญในผู้ป่วยไอทีพี

วัสดุและวิธีการ: ผู้นิพนธ์ได้วิเคราะห์ข้อมูลผู้ป่วยในที่ได้รับการวินิจฉัยว่าเป็นโรค ไอทีพี ตามรหัส ICD-10 คือ D69.3 ซึ่งได้ข้อมูลจากระบบประกันสุขภาพทั่วประเทศในปี พ.ศ. 2553 ข้อมูลถูกวิเคราะห์ตามกลุ่มอายุ เพศและระบบประกันสุขภาพ

ผลการศึกษา: อัตราการนอนโรงพยาบาลและอัตราการเสียชีวิตรวมคือ 7.68 และ 0.29 ต่อประชากร 100,000 คน ตามลำดับ และเพิ่มขึ้นตามอายุโดยพบในผู้หญิงมากกว่า ค่ารักษาพยาบาลและระยะเวลาในการนอนโรงพยาบาลเฉลี่ยคือ 27,133 บาท และ 6.7 วันต่อครั้ง ตามลำดับ และผู้ชายสูงกว่าผู้หญิงเล็กน้อย โรคที่พบร่วมบ่อยที่สุดคือโรคความดันโลหิตสูง ภาวะเลือดออกในทางเดินอาหารเป็นภาวะเลือดออกที่พบบ่อยที่สุดโดยพบ 21.5 ครั้งต่อการนอนโรงพยาบาล 1,000 ครั้ง ผู้ป่วยในระบบประกันสุขภาพแบบเบิกจ่ายตรงมีร้อยละของการเข้าถึงการรักษา ราคาสูงมากที่สุด

สรุป: อัตราการนอนโรงพยาบาล อัตราการเสียชีวิตและภาวะเลือดออกที่สำคัญเพิ่มขึ้นตามอายุและพบในผู้หญิงมากกว่าผู้ชาย ค่ารักษาพยาบาลและระยะเวลาในการนอนโรงพยาบาลเฉลี่ยสูงในผู้ชายมากกว่าผู้หญิง โรคที่พบร่วมอาจสัมพันธ์กับการรักษาไอทีพี มีความแตกต่างกันในการเข้าถึงการรักษาราคาสูงระหว่างระบบประกันสุขภาพ
