

Epidemiology of primary and secondary thrombocytopenia: first analysis of an administrative database in a major Italian institution

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Administrative databases can be a reliable source for estimating the epidemiology of blood disorders. No data are available estimating the epidemiology of thrombocytopenia from administrative data in Italian institutions. We analyzed the administrative database of the Padua University Hospital with the aim to study the epidemiology of thrombocytopenia in patients discharged with an International Classification of Disease, 9th Revision, Clinical Modification (ICD9-CM) code of thrombocytopenia. The database from year 2004 to 2008 was evaluated and all cases of thrombocytopenia (Code 287.1, 3, 4, 5) were identified and analyzed with regard to age, sex, associated diseases, therapeutics procedures and bleeding complications. The accuracy of electronic records was validated in all available medical records of patients discharged in 2009, by applying the ICD9-CM update 2007 version (Code 287.1, 4, 5; 287.30, 31, 32, 33, 39). We found 368 patients discharged from 2004 to 2008 with an ICD9-CM code of thrombocytopenia, correspondent to 0.1% of discharge rate and to a rate of 73.6 patients/year. The incidence of thrombocytopenia for this period was 14.8 cases per 100 000 per year. When considering patients with an ICD9-CM diagnosis of immune thrombocytopenia (ITP: Code 287.3), the incidence was of 6.8 cases per

100 000 per year. The clinical records of 40 patients with a discharge diagnosis of thrombocytopenia during year 2009 were reviewed for clinical consistency with ICD9-CM codes. A concordant diagnosis between clinical records and discharge code was found in 82.5% of cases. Following validation of ICD9-CM code, the incidence of ITP (Code 287.31) was 2.6 cases per 100 000 per year. When evaluated for sensitivity and specificity, we found the ICD-9-CM to be useful in studying thrombocytopenia using administrative data. *Blood Coagul Fibrinolysis* 23:271–277 © 2012 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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Introduction

Administrative healthcare databases provide an increasingly accessible and widely used source of data for healthcare research [1]. However, the accuracy of hospital discharge data remains uncertain. When administrative healthcare databases are exploited to study the epidemiology of multiple diseases, two clinical questions should be addressed: first, whether a specific medical situation present in the patient was coded on the electronic record and whether a specific medical situation coded on the electronic database was present in the patient. An alternative use of administrative databases is in population-based studies of specific conditions or coded treatments. In this setting, the accuracy of coding for specific medical conditions is higher and, therefore, they can be reliably identified by the administrative database [2].

Previous studies have evaluated the reliability of administrative databases in estimating the epidemiology of blood disorders. Particularly, idiopathic thrombocytopenic

purpura has been considered by several authors [3–5]. However, no data are available describing the epidemiology of thrombocytopenia by analysis of administrative data in Italian institutions.

In this article, we have studied the epidemiology of thrombocytopenia by identifying patients discharged from an Italian University Hospital with a diagnosis of thrombocytopenia according to the International Classification of Disease, 9th Revision, Clinical Modification (ICD9-CM) and to the updated version introduced in 2007. Validation of electronic database was also performed by clinical records in the subgroup of patients discharged in 2009 following the latest ICD9-CM update.

Material and methods

This was a cross-sectional study of inpatients receiving care at a tertiary care hospital. We reviewed the electronic medical records of ordinary hospitalizations (Qlik, Padova University Hospital) from the year 2004 to 2008 for patients discharged with a ICD9-CM code related to

Table 1 ICD9-CM codes for thrombocytopenia used in Italy during 2004–2008 (ICD9-CM 1997) and 2009 (ICD9-CM 2007)

ICD9-CM 1997	Definition	ICD9-CM 2007	Definition
287.1	Thrombocytopathy	287.1	
287.3	Primary (immune)	287.30	Primary unspecified
		287.31	Immune
		287.32	Evans'
		287.33	Congenital
		287.39	Others primary
287.4	Secondary	287.4	Secondary
287.5	Unspecified	287.5	Unspecified

ICD, International Classification of Disease.

any thrombocytopenic medical condition as primary or secondary diagnoses (287.1, 287.3, 287.4, 287.5) (Table 1). Immune thrombocytopenia (ITP) has been identified with Code 287.3. This database contains detailed information with regard to patient demographics, description of the nature of the admission, discharge disposition, diagnostic and procedure codes. In addition, based on ICD9-CM coding at discharge, we retrieved information about concomitant diagnosis, therapeutic interventions related to thrombocytopenia (transfusions, intravenous immunoglobulins, splenectomy), hemorrhagic events and mortality. Only the first-episode hospitalization for each individual was considered.

Verification of diagnosis

For all patients discharged in 2009 with an ICD9-CM coded diagnosis of thrombocytopenia (287.1, 287.30–39, 287.4, 287.5) (Table 1), the correctness of the specific diagnosis was determined by carefully analyzing all available clinical charts of ordinary admissions. For all specific causes of thrombocytopenia, we evaluated the clinical history and physical examination of the patient, their clinical course (also according to the treatment given), the results of laboratory investigations, particularly those regarding the blood smear, abdominal ultrasound scanning for spleen size and bone marrow examination when available. For a diagnosis ITP, current published guidelines were followed [6] to validate the code 287.31.

Data analysis

Incidence was estimated by considering the mean rate of hospital admission in the Veneto region from 2004 to 2008 and in 2009 (equal to 137.2 per 1000 and 121.1 per 1000, respectively) (http://www.regione.veneto.it/Servizi+alla+Persona/Sanita/Libro+Bianco+2000_2009.html). We calculated the sensitivity and the positive predictive value of billing code 287.31 for identifying patients with ITP. Sensitivity was calculated as the number of patients coded with 287.31 divided by the total number of patients identified as having ITP in the medical records. The positive predictive value was calculated as the percentage of patients who truly have ITP and were correctly coded as such, divided by the total number of patients who were billed as code 287.31.

Results

Over the 5 years of analysis (2004–2008), 338 880 patients were discharged from Padova University Hospital. The number of patients first diagnosed with an ICD9-CM code for thrombocytopenia was 368 (235 as a primary diagnosis, 133 as a secondary diagnosis) corresponding to 0.1% of discharge rate and to 73.6 patients/year. The male/female ratio of patients discharged with a diagnosis of thrombocytopenia was 0.83 (167 vs. 201, respectively). The frequency and distribution of ICD9-CM diagnosis are shown in Fig. 1.

The incidence of thrombocytopenia was 14.8 cases per 100 000 per year, with an ITP incidence (Code 287.3) of 6.8 cases per 100 000 per year.

Considering all cases with an ICD9-CM code for thrombocytopenia, average length of in-hospital stay was 5.8 days. When considering age of patients (only the database from 2004 to 2007 was considered as our hospital system did change age subgroups, therefore making 2008 inclusion problematic), 126 patients (39%) were more than 60 year old, whereas an equal distribution was observed among patients younger than 18 years (22.1%), between 18 and 39 (21.5%) and from 40 to 60 years (15.3%) (Fig. 2).

Considering patients with 287.3 discharge code (ITP), 50 patients (32%) were younger than 18 years, and 43 patients (28%) were more than 60 years old.

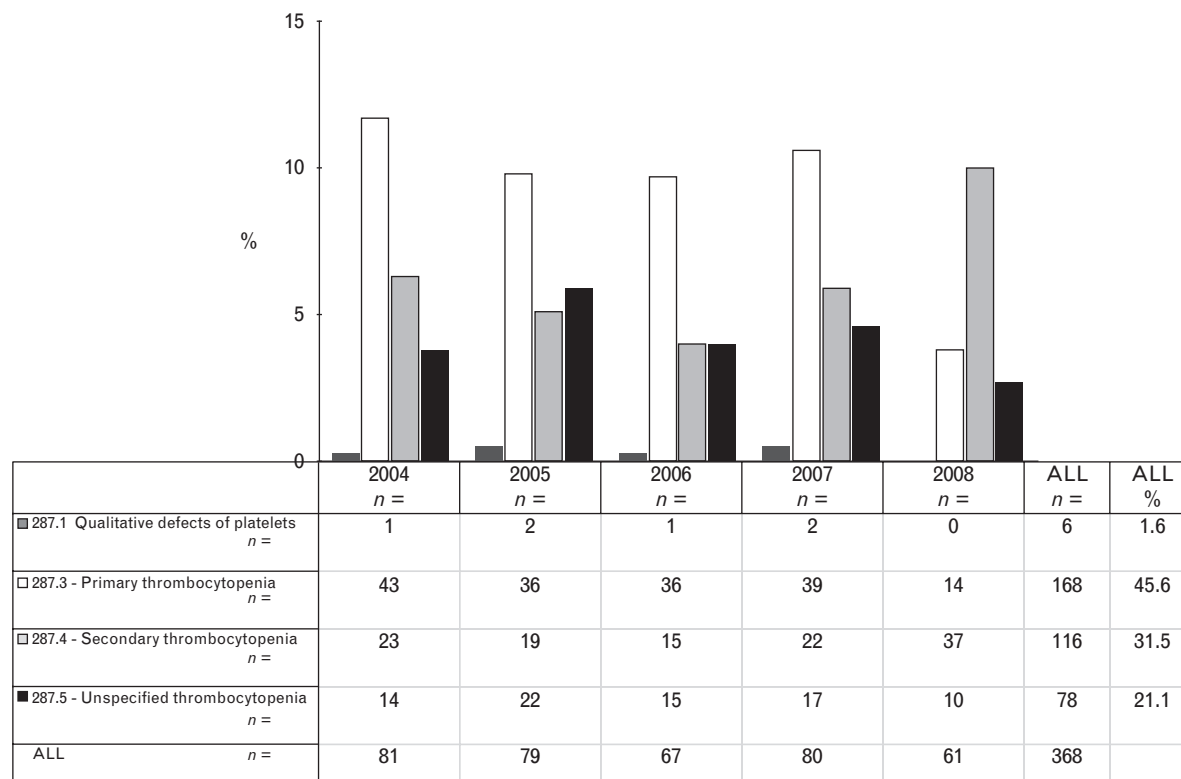
We also examined the functional discharge area (Fig. 3). Two hundred and three patients (55.1%) were discharged from a medical ward, 65 (17.6%) from the pediatric ward, 74 (20.1%) from the oncohematology unit, 22 (5.9%) from a surgical ward and four (1%) patients from the cardiovascular unit.

We then analyzed the concomitant discharge ICD-grouped diagnosis associated to an ICD9-CM code of thrombocytopenia. We found a rather heterogeneous pattern of diagnosis as shown in Table 2. One hundred and six patients (28.8%) were not linked to any secondary diagnosis, whereas all other 100 patients (27.1%) had a diagnosed included in other ICD9-CM disorders not diagnosed as above (see legend to Table 2).

We then considered therapeutic interventions in the setting of thrombocytopenia that were recorded in the discharge card. Sixty-five patients (17.6%) received a treatment including splenectomy (12 cases), blood or platelet transfusion (31 patients), immunoglobulins (18 patients) or plasma exchange (four patients). Thirty-eight of 65 patients who received any of the above-mentioned treatment had the ICD9-CM code 287.3, ITP.

Hemorrhagic events were also considered by screening the database for codes consistent with bleeding episodes. Only 28 cases (7.6%) were coded as associated to a bleeding episode, equally distributed between males

Fig. 1



Distribution of an International Classification of Disease (ICD9-CM) codes for thrombocytopenia from 2004 to 2008.

and females. Six of 28 cases were diagnosed with ITP code. Interestingly, 20 of the 28 patients (71.4%) who experienced bleeding were at least 60 years old.

The mortality rate in our cohort of patients was 2.7% with a male/female ratio of 1:9. None of the 10 died patients received a code related to a bleeding episode.

As mentioned in the Methods section, the ICD9-CM was updated in 2009. In the new version, code 287.3 was implemented to more accurately include distinct forms of primary thrombocytopenia (Table 1).

There were 65 146 patients discharged from ordinary hospitalization. A total of 47 patients (0.07%) were discharged with a code referring to thrombocytopenia. Twenty-three of 47 patients (48.9%) received a new subcode from the updated ICD9-CM. Particularly, nine patients were coded with 287.30 and 14 patients with Code 287.31.

When considering these 23 cases, the male/female ratio was 0.9 (11 vs. 12), with a mean age of 37.5 ± 29.9 and 33.4 ± 32.4 years for females and males, respectively.

The incidence of thrombocytopenia in 2009 was then 8.75 cases per 100 000 per year, lower than 14.8 cases per

100 000 per year observed in the previous analysis of 2004–2008.

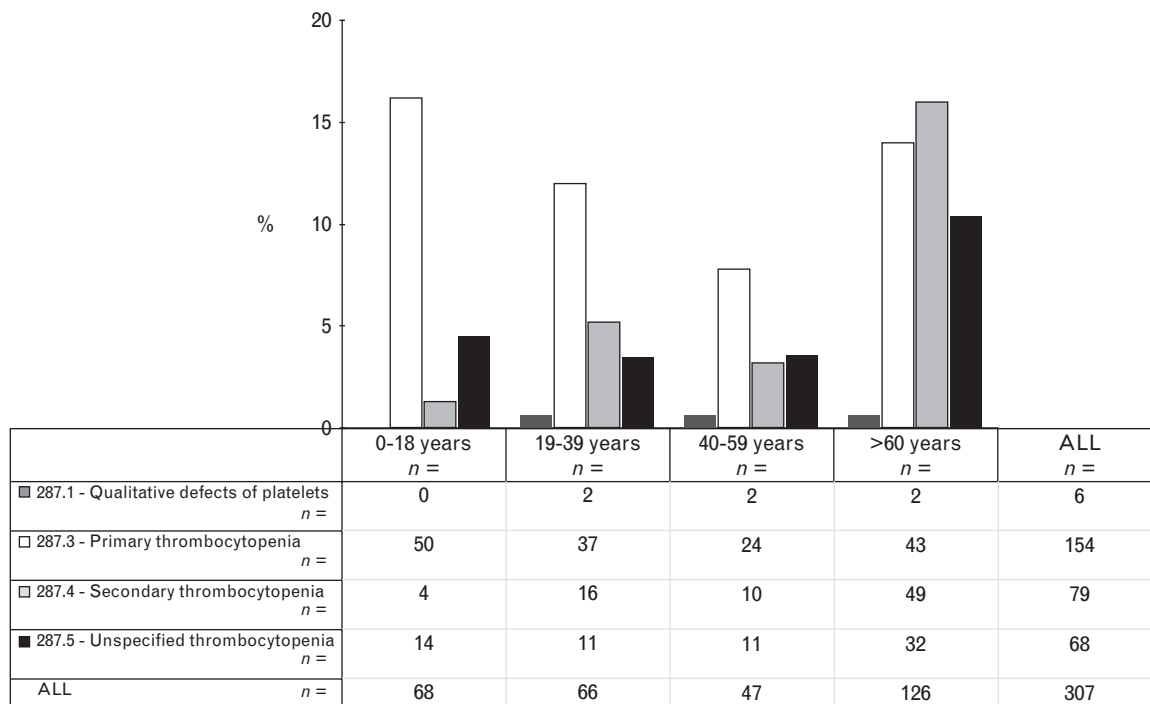
Validation of diagnoses

The clinical records of 40 of 47 patients with a discharge diagnosis of thrombocytopenia were available for review. Consistency between diagnosis at discharge and ICD9-CM was verified in 14 patients coded 287.4, four patients coded 287.5, eight patients coded 287.30 and 14 patients who received the Code 287.31.

Overall, a concordant diagnosis between clinical records and discharge code was found in 33 of 40 (82.5%) patients. Two patients had an incorrect diagnosis of ITP, whereas four patients with a different code of thrombocytopenia had ITP (Code 287.31).

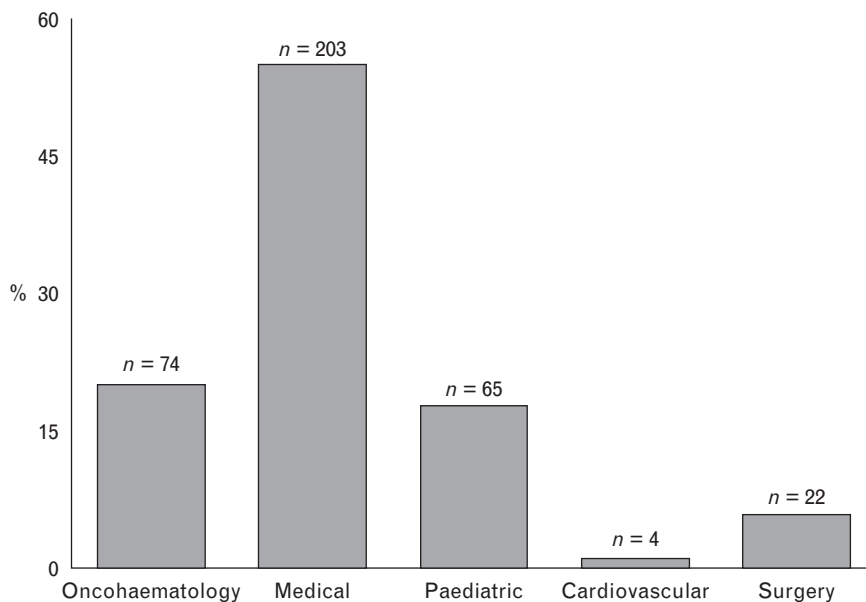
Specificity and sensitivity of Code 287.31 was calculated. Sensitivity of the code for identifying patients with ITP was 80% (95% confidence interval 0.51–0.94). This is a conservative estimate of sensitivity because of how the patients with other coded diagnoses were selected. The specificity of this code was 88% (95% confidence interval 0.67–0.96). The positive predictive value of a diagnosis coded 287.31 is 80% (95% confidence interval 0.56–0.97)

Fig. 2



Distribution of patients discharged with an International Classification of Disease (ICD9-CM) code of primary thrombocytopenia according to age (only database from 2004 to 2007).

Fig. 3



Distribution of patients discharged with an International Classification of Disease (ICD9-CM) code of thrombocytopenia according to clinical specialty.

Table 2 Secondary diagnoses coded accordingly to an International Classification of Disease (ICD9-CM) in thrombocytopenic patients

ICD9-CM codes	287.1	287.3	287.4	287.5	Total
Infectious and parasitic diseases (001–139)	–	15	4	5	24 (6.5%)
Neoplasms (140–239)	–	5	28	8	41 (11.1%)
Diseases of the blood (280–289)	–	5	22	14	41 (11.1%)
Diseases of the circulatory system (390–459)	1	13	10	4	28 (7.6%)
Diseases of the digestive system (520–579)	1	7	10	10	28 (7.6%)
Not coded		79	12	15	106 (28.8%)
Others ^a	4	44	30	22	100 (27.1%)
Total	6	168	116	78	368

^aOthers include codes 279: endocrine, nutritional, metabolic and immunity disorders; 290–319: mental disorders; 320–389: diseases of the nervous system and sense organs; 460–519: diseases of the respiratory system; 580–629: diseases of the genitourinary system; 630–679: complications of pregnancy, childbirth and the puerperium; 680–709: diseases of the skin and subcutaneous tissue; 710–739: diseases of the musculoskeletal system and connective tissue; 780–799: symptoms, signs and ill-defined conditions; 800–999: injury and poisoning; and V01–V83: supplementary classification of factors influencing health status and contact with health services.

and the negative predictive value is 88.4% (95% confidence interval 0.68–0.96%).

We then evaluated the hemorrhage episodes according to platelet count in all available patients (Table 3) [7]. A 32.5% of patients were asymptomatic, 57.5% experienced minor hemorrhages, whereas 7.5% were reported as suffering grade 2 bleeding. One patient (2.5%) with severe thrombocytopenia died of cerebral hemorrhage. Thirty-two of 40 patients (80%) presented with a platelet count below 30×10^9 cells/l and received a treatment for thrombocytopenia (Table 3).

Following the clinical validation of ICD9-CM code at discharge during 2009, the incidence of Code 287.31 (ITP) was 2.6 cases per 100 000 per year. That incidence was lower than 6.78 cases per 100 000 per year obtained in the previous analysis of 2004–2008 using the generic Code 287.3 ‘primary thrombocytopenia’.

Discussion

This is the first Italian study evaluating the epidemiology of thrombocytopenia in a cohort of patients discharged from an academic hospital by using administrative database. All electronic records of patients discharged with a

thrombocytopenic condition coded according to ICD9-CM were considered.

On the basis of electronic data, we have defined the incidence of thrombocytopenia as coded accordingly to ICD9-CM in patients discharged from our University Hospital from year 2004 to 2008. Moreover, we also evaluated the relationship between age, sex, severity of bleeding, treatment and the thrombocytopenia code at discharge.

We found that thrombocytopenia was diagnosed in 0.1% of all patients discharged in the 5-year period from our University Hospital.

The most frequent diagnosis was the code of primary thrombocytopenia (ICDM9-CM 1997, Code 287.3) that has been validated for the diagnosis of ITP [8]. As previously reported, we found a higher incidence of thrombocytopenia in older patients and in females [9,10]. Particularly, we found a higher incidence of this subcode in young individuals or in patients above 60 years.

These results are consistent with the prevalence of acute ITP in younger age and chronic form in adults [10,11].

Table 3 Hemorrhage severity (WHO grading) and treatment according to range of thrombocytopenia

Platelet count, $\times 10^9$ cells/l	Grade 0	Grade 1	Grade 2	Grade 4	Total	Treated (n)
50–100	5	1	/	/	6	S (4)
30–50	2	/	/	/	2	S + IVIGG (1)
10–30	4	11	2	/	17	S (2) PC (8) IVIGG (4) S + PC (1) S + PC + IVIGG (1) IVGG + PC (1)
<10	2	11	1	1	15	S (2) IVIGG (3) S + IVIGG (2) IVIGG + PC (4) S + PC + IVIGG (3) S + PC + IVGG + RBC (1)
Total	13	23	3	1	40	

IVIG, intravenous immunoglobulins; PC, platelet concentrates; RBC, red blood cells; S, corticosteroids. Data from [7].

Forty-three percent of thrombocytopenic patients have been discharged from medical wards, whereas 23% from the pediatric department; the same proportion was found when considering the Code 287.3 that identifies ITP. When analyzing electronic data for appropriateness in hospital admission of ITP patients according to American Society of Hematology guidelines [12], only 26% of patients had electronic codes justifying admission as platelet transfusion, bleeding or immunoglobulin therapy. Of interest, mean hospital stay of ITP patients was 5.8 days, well below the average for all hospital admission that is about 8 days. Only 6% of patients with an ICD9-CM code of ITP were splenectomized, according to the correspondent code. This result is in agreement with Schoonen *et al.* (6.1%) [4] and lower than Neylon *et al.* (12%) [9]. However, this data can be underestimated, as we may have missed a significant proportion of patients with a code of splenectomy not having a concordant ICD9-CM code of thrombocytopenia. In agreement with the literature data, this data may also support that splenectomy is more frequently deferred compare to the past [10]. Overall mortality was 2.7% and it was higher in female, as already found in previous studies [13]. None of patients who died with thrombocytopenia were coded with an ICD9-CM consistent with a major bleeding episode.

To evaluate the accuracy of ICD9-CM codes in consistently identifying thrombocytopenia, we validated the electronic records of patients discharged in 2009 by evaluation of 86% of patients discharged with an ICD9-CM code of thrombocytopenia. On the contrary, the 2009 updated version of the ICD9-CM code allowed a more accurate subcoding of ITP by Code 287.31. Also, 82.5% of patients showed an ICD9-CM code concordant with the clinical diagnosis of thrombocytopenia and 80% have platelets less than 50×10^9 cells/l, confirming the appropriateness of admission [10]. Therapeutic intervention was properly related to the severity of thrombocytopenia and to bleeding symptoms as previously reported [14]. Mortality related to bleeding was 2.5%, confirming the data obtained from analysis of previous years.

However, only 14% of cases had an appropriate code referring to the therapeutic intervention compared with 53% of patients with a clinical record defining it. This suggests that electronic database may be inappropriate to define the epidemiology of therapeutic interventions in the setting of thrombocytopenia.

Finally, in this validated group of patients, we found an ITP incidence of 2.6 cases per 100 000 per year in agreement with Frederiksen and Schmidt [15,16], but slightly higher than reported by Neylon *et al.* [9]. The comparison is probably biased by the inclusion of patients only with a platelet count less than 50×10^9 cells/l in the study by Neylon *et al.* When estimating, prevalence of thrombocytopenia that is generated using administrative data will somewhat overestimate true disease prevalence.

The results are concordant with studies that have evaluated other diagnostic codes and report reasonable, although imperfect, accuracy of ICD-9-CM codes in administrative data [2,7,17,18]. However, this study has several limitations, particularly related to the relatively small numbers of records available for patients discharged in 2009 with a diagnosis of thrombocytopenia. Consequently, the assumption that data from the 2009 database reflect the accuracy of ICD9-CM coding in the period 2004–2008 would be inappropriate. Also, ICD9-CM codes for specific thrombocytopenia such as ITP were not available until 2007. As a result of this update in ICD9-CM classification, one may expect a drop in newly coded thrombocytopenia subtypes such as ITP, therefore making comparison between the different coding systems unreliable. This is supported by our results as we found an ITP incidence in 2009 more than two times lower compared with the incidence of ITP in the 2004–2008 period. This is in contrast with previous studies reporting that the specificity between the two ICD9-CM codes was not significantly different in identifying ITP [8]. However, one may surmise that over time ITP patients are actually more treated as outpatients, therefore influencing the true incidence of this condition when limited to hospitalized patients.

In conclusion, administrative databases may offer a reliable tool in the evaluation of epidemiology of thrombocytopenia. However, this approach has limitations particularly when analyzing therapeutic interventions in the setting of thrombocytopenia.

Acknowledgements

Conflicts of interest

The authors declare no conflict of interest.

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