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Abstract

Background: Thrombocytopenia is a frequently encountered laboratory abnormality and a common reason for hematology referrals. Workup for thrombocytopenia is not standardized and frequently does not follow an evidence-based algorithm. We conducted a systematic analysis to evaluate the laboratory testing and outcomes of patients evaluated for thrombocytopenia at hematology clinics in a tertiary referral center between 2013 and 2016.

Patient and methods: We performed a comprehensive chart review for patients evaluated for thrombocytopenia during the study period. Patients were followed for 1 year from the initial hematology evaluation and assessed for the development of a hematologic malignancy, rheumatologic, or infectious diseases among other clinical outcomes.

Results: We evaluated 472 patients with a median (range) age of 61 (17−94) years. The majority (63.8%) had mild thrombocytopenia. Within 1 year of follow-up, 14 patients (3.0%) were diagnosed with a hematologic malignancy. A higher likelihood of developing a hematologic malignancy was noted in patients with concurrent leukopenia (hazard ratio [HR] 9.97, 95% confidence interval [CI] 3.28−30.32, $p < .01$) and increasing age (HR per 10-year deciles 1.52, 95% CI 1.03−2.25, $p = .03$). In patients with asymptomatic isolated mild thrombocytopenia, laboratory testing did not reveal any significant positive findings and patients did not receive any new major diagnosis during the follow-up period.

Conclusion: Our findings provide basis and call for development of an evidence-based algorithmic approach for evaluation of patients with thrombocytopenia, testing, and referrals. It also supports a conservative approach mainly driven by physical exam signs, symptoms, and other laboratory findings for patients with isolated mild thrombocytopenia.

Keywords: Hematology, Malignancy, Platelets, Referrals, Thrombocytopenia

1. Introduction

The normal adult platelet count range is 150−450 × 10^9/L, with mean values of 266 × 10^9/L and 237 × 10^9/L in females and males, respectively [1]. Thrombocytopenia, defined as platelet count <150 × 10^9/L, is a frequent reason for hematology consultation as it can be associated with life-threatening complications (such as bleeding or even thrombosis; e.g., heparin-induced thrombocytopenia) and also due to concerns about underlying hematologic malignancies, especially when accompanied by other abnormal blood counts [2,3].

Furthermore, extensive laboratory testing is usually ordered in an attempt to determine the underlying pathology. The workup could potentially range from repeating a complete blood count (CBC) and performing a peripheral smear to an extensive evaluation for an underlying infectious, rheumatologic, or malignant disorder.

We conducted this study to evaluate the laboratory testing initiated by hematologists for patients with thrombocytopenia, as well as the baseline characteristics associated with certain clinical outcomes in these patients, as a step towards a standardized approach and evidence-based referral and testing algorithms.

2. Methods

2.1. Patients

After obtaining approval of the Institutional Review Board at Henry Ford Health System (Detroit, MI, USA), we searched for outpatient hematology referrals with a diagnosis of thrombocytopenia using International Classification of Diseases (ICD-9) and (ICD-10) diagnostic codes for thrombocytopenia (ICD-9 codes: 287.5, 287.31, 287.49; ICD-10 codes: D69.6, D69.59) in Henry Ford Hospital (Detroit, MI, USA) database between June 1, 2013 and June 1, 2016. Data collected included patient demographics, clinical symptoms and bleeding history, history of hematologic, rheumatologic, infectious, and chronic liver diseases, medications, the presence of other abnormalities on CBC, and laboratory testing performed to investigate the thrombocytopenia at the time of presentation. Patients were followed for a period of 1 year from the first visit with a hematologist (index visit) and were assessed for development/diagnosis of any of the following outcomes: hematologic malignancy, rheumatologic disorder, infectious disease, or bleeding. Patients were excluded if they had any of the following: known hematologic disorder or malignancy, ongoing chemotherapy, or if they were seen by a hematologist prior to the index visit for a platelet-related disorder.

2.2. Definitions

Mild, moderate, and severe thrombocytopenia were defined as a platelet count of $100-150 \times 10^9$/L, $50-99 \times 10^9$/L, and $<50 \times 10^9$/L, respectively. For patients to be classified under any category, they had to have at least two values in the pre-specified range within the previous year. If a patient had platelet counts that met the criteria for more than one category, they were considered to be in the more severe category (e.g., if the patient had two values in the mild thrombocytopenia range and two values in the moderate thrombocytopenia range, they would be classified as having moderate thrombocytopenia). Only laboratory tests or imaging studies that were performed in more than 5% of patients were included in the analysis. "Explanation for thrombocytopenia at 1 year" was defined as a new diagnosis of hematologic malignancy, immune thrombocytopenic purpura, thrombotic thrombocytopenic purpura, new solid cancer diagnosis, prior or new liver disease, prior or new rheumatologic disease, infection (e.g., HIV), nutritional deficiency, pregnancy, end-stage renal disease, drug effect, spurious result (EDTA-related clumping), or multiple of these contributing factors.

2.3. Statistical analysis

For the outcomes of "new diagnosis of hematologic malignancy" and "explanation of thrombocytopenia at 1 year", a logistic regression model was created and odds ratios (ORs) were calculated for covariates that were present at the time of the index visit. Variables with $p < .10$ in univariate analysis were included in multivariate models. Age was included as a continuous variable parsed into decades (age 10−19 years, 20−29 years, etc.). ORs and 95% confidence intervals (CIs) are reported for the logistic regression analyses. Fisher's exact test was used to compare categorical variables, where appropriate. Statistics were calculated using JMP version 14.0, SAS Institute Inc., Cary, NC.

3. Results

We evaluated 580 patients for thrombocytopenia during the study period. Of 580 patients, 108 were excluded due to loss to follow-up, known hematologic disorder or cancer, or prior known platelet-related disorder. The remaining patients ($n = 472$) constituted our cohort with a median (range) age of 61 (17−94) years, and 282 patients (59.7%) were males. The majority of patients ($n = 274$, 58.1%) were white, followed by African American ($n = 140$, 29.7%) and others ($n = 58$, 12.3%). Regarding the severity of thrombocytopenia, 301 patients (63.8%) had mild thrombocytopenia, 135 patients (28.6%) had moderate thrombocytopenia, and 36 patients (7.6%) had severe thrombocytopenia. Of the entire cohort, 68 patients (14.4%) were known to have chronic liver disease (alcoholic, nonalcoholic, or viral) and 34 patients (7.2%) had a history of autoimmune/rheumatologic disease. Sixty patients (12.7%) were on a medication known to cause thrombocytopenia within a 3-month period prior to the index visit [4−6]. Chronicity of thrombocytopenia at the time of index visit was divided into three time periods (<1 years, 1−5 years, and >5 years), with 35.8%, 36.5%, and 27.7% of patients falling in each of these categories, respectively. Patient characteristics parsed according to the severity of thrombocytopenia are shown in Table 1.

Sixty-seven patients (14.2%) had concurrent leukopenia (defined as white blood cell count $<3.5 \times 10^9$/L) and 130 patients (27.5%) had concurrent anemia (defined as hemoglobin < 13.5 g/dL in men and < 12 g/dL in women). The majority of patients ($n = 388$, 82%) had no history of bleeding

Table 1. Patient characteristics.

Patient characteristics		Mild thrombocytopenia (N = 301)	Moderate thrombocytopenia (N = 135)	Severe thrombocytopenia (N = 36)
Sex	Male	189 (62.8)	71 (52.6)	22 (61)
	Female	112 (37.2)	64 (47.4)	14 (39)
Race	White	172 (57.1)	84 (62)	18 (50)
	African American	86 (28.6)	39 (29)	15 (42)
	Hispanic	9 (3)	1 (0.7)	2 (5)
	Asian	9 (3)	4 (3)	0 (0)
	Other/unknown	25 (8.3)	7 (5)	1 (3)
Age (yr)	18−40	60 (20)	16 (11.8)	3 (8)
	41−65	130 (43.1)	71 (53)	19 (53)
	>65	111 (36.9)	48 (35)	14 (39)
History of liver disease		21 (7)	36 (26.6)	11 (30)
History of autoimmune disease/rheumatologic disease		20 (6.6)	10 (7.4)	4 (11)
Medications known to cause thrombocytopenia		41 (13.6)	15 (11)	4 (11)
Chronicity of thrombocytopenia (yr)[a]	<1	117 (38.8)	38 (28.1)	14 (38.9)
	1−5	110 (36.5)	49 (36.2)	13 (36.1)
	>5	74 (24.5)	48 (35.5)	9 (25)
Concurrent leukopenia[b]		38 (12.6)	21 (15.5)	8 (22.2)
Concurrent anemia[c]		57 (19)	53 (38.5)	20 (55.5)
Symptoms[d]		26 (8.6)	43 (31.8)	15 (41.6)

Note. Data are presented as n (%).

[a] An exhaustive list that was adapted from the following references was used to identify medications that can potentially cause thrombocytopenia [4−6].

[b] Defined as a white blood cell count < 3.5×10^9/L.

[c] Defined as haemoglobin <13.5 g/dL in men and <12 g/dL in women.

[d] Symptoms include mucosal bleeding (e.g., mouth, nose, urinary tract, and gastrointestinal tract), bruising or subcutaneous bleeding (petechial, purpura, ecchymosis), and musculoskeletal bleeding. The presence of symptoms was determined based on history rather than an objective assessment by healthcare provider.

(mucosal bleeding [e.g., mouth, nose, urinary tract, and gastrointestinal tract], bruising or subcutaneous bleeding [petechial, purpura, ecchymosis], and/or musculoskeletal bleeding); however, a significantly increased incidence of bleeding symptoms was noted with increasing severity of thrombocytopenia (8.6%, 31.9%, and 41.7% for mild, moderate, and severe thrombocytopenia, respectively; $p < .01$).

3.1. Laboratory testing

Workup ranged from repeating a CBC to a battery of tests aimed at finding an underlying pathology (including but not limited to peripheral smear, testing for HIV, viral hepatitis serology, antinuclear antibody [ANA], rheumatoid factor [RF], iron profile [iron, ferritin, total iron binding capacity], vitamin B12 and folic acid levels, abdominal ultrasound to evaluate for splenomegaly, protein electrophoresis, immunofixation and immunoglobulin levels, and bone marrow biopsy).

The most commonly performed tests (>5% of patients) for each thrombocytopenia severity category and percentage of abnormal results are shown in Table 2. The most frequently performed test was vitamin B12 level; checked in 337 patients (71.4%)

and returned abnormal in only 18 of those patients (5.3%). This was followed by ANA; ordered for 328 patients (69.5%) with 60 abnormal results (18.3%). Bone marrow biopsies were performed in 8%, 16.2%, and 63.8% in patients with mild, moderate, and severe thrombocytopenia, respectively.

3.2. Outcomes

At the 1-year follow-up mark, 14 patients (3.0%) were diagnosed with a hematologic malignancy as the following: chronic lymphocytic leukemia/small lymphocytic lymphoma ($n = 4$), large granular lymphocyte leukemia ($n = 2$), multiple myeloma ($n = 2$), myelodysplastic syndrome ($n = 2$), chronic myelomonocytic leukemia ($n = 1$), low-grade B-cell lymphoma ($n = 1$), marginal zone lymphoma ($n = 1$), and T-cell acute lymphoblastic leukemia ($n = 1$). In a multivariate logistic regression model, patients with concurrent leukopenia (OR 9.97, 95% CI 3.28−30.32, $p < .01$) and increased age (OR 1.52 per decade, 95% CI 1.03−2.25, $p = .03$) had a significantly increased relative odds of having a newly diagnosed hematologic malignancy at 1 year (Table 3). Of note, all 14 patients diagnosed with a hematologic malignancy had other constitutional symptoms, signs, abnormal

Table 2. Workup for Thrombocytopenia.

Test	Mild thrombocytopenia (N = 301)		Moderate thrombocytopenia (N = 135)		Severe thrombocytopenia (N = 36)	
	Tested; n (%)	Abnormal result; n (% of tested)	Tested; n (%)	Abnormal result; n (% of tested)	Tested; n (%)	Abnormal result; n (% of tested)
ANA	205 (68)	32 (15.6)	94 (69.6)	20 (21)	29 (80.5)	8 (27.5)
Vitamin B12	200 (66)	7 (3.5)	108 (80)	7 (6.5)	29 (80.5)	4 (13.8)
MPEV	158 (52)	12 (7.5)	86 (63.7)	0 (0)	26 (72)	0 (0)
RF	150 (50)	5 (3.3)	68 (50)	4 (6)	24 (66.6)	2 (8.3)
Viral hepatitis serology	147 (49)	5 (3.4)[a]	85 (63)	10 (12)[b]	31 (86)	6 (19.3)[c]
Iron profile	114 (38)	16 (14)	78 (57.7)	20 (25.6)	25 (69.4)	7 (28)
Abdomen ultrasound	112 (37)	26 (23)	83 (61.4)	25 (30)	30 (83.3)	9 (30)
HIV	101 (33)	1 (0.3)	55 (40.7)	0 (0)	21 (58.3)	0 (0)
Peripheral smear	73 (24)	2 (2.7)	51 (37.7)	6 (11.7)	19 (52.7)	4 (21)
Bone marrow biopsy	24 (8)	5 (21)	22 (16.2)	5 (22.7)	23 (63.8)	3 (13)

Note. ANA = antinuclear antibodies; HIV = human immunodeficiency virus; MPEV = monoclonal protein evaluation; RF = rheumatoid factor.

[a] Four patients had a known history of chronic viral hepatitis (hepatitis B or C).
[b] Eight patients had a known history of chronic viral hepatitis (hepatitis B or C).
[c] Five patients had a known history of chronic viral hepatitis (hepatitis B or C).

blood counts, and/or imaging studies besides thrombocytopenia that warranted further workup at time of initial evaluation (Table 4).

Five patients (1.1%) were diagnosed with a new infectious disease: hepatitis B/C (n = 3), HIV (n = 1), and infectious mononucleosis caused by Epstein−Barr virus (n = 1). One patient (0.2%) had a new rheumatologic diagnosis (mixed connective tissue disease). Six patients (1.3%) had minor bleeding (cutaneous bruising, mild menorrhagia, and hemorrhoidal bleeding); no patients had significant bleeding that required transfusion of blood products. Other notable hematologic diagnoses included 20 patients with immune thrombocytopenic purpura, 10 patients with monoclonal gammopathy of undetermined significance, and one patient with thrombotic thrombocytopenic purpura. Six patients (1.3%) were diagnosed with solid malignancies as the result of further workup. Two patients (0.4%) had newly diagnosed nonalcoholic fatty liver disease diagnosed after further workup.

Taken together, 192/472 patients (40.7%) had a putative explanation for thrombocytopenia after 1 year of follow-up (Fig. 1), whereas 280/472 patients (59.3%) did not develop any new clinical condition or have any identified underlying factor that could explain the thrombocytopenia within 1 year of the index visit. In a multivariate logistic regression model for explanation for thrombocytopenia at 1 year, severity of thrombocytopenia had a significantly higher relative odds of explanation (moderate/severe vs. mild, OR 2.30, 95% CI 1.52−3.48, $p < .01$) after adjusting for symptoms at the index visit and concurrent anemia, which were both significant in univariate analysis (Table 3).

4. Discussion

Hematology referrals for thrombocytopenia constitute a significant portion of patients seen in a general hematology clinic. In our study, we examined the laboratory testing and clinical outcomes for 472 patients who were evaluated for thrombocytopenia in hematology subspecialty clinics at a tertiary center. We noted that having moderate to severe thrombocytopenia ($<99 \times 10^9$/L) was associated with a higher likelihood of having an explanation for thrombocytopenia at 1 year. We also noted that both having concurrent leukopenia along with thrombocytopenia and increasing age significantly increased the relative odds of receiving a diagnosis of a hematologic malignancy within 1 year and a more extensive and invasive workup (i.e., bone marrow biopsy, etc.) can be considered in such patients. It is also important to note that the majority of patients (280/472 [59.3%]) did not have any explanation for their thrombocytopenia at the 1-year mark.

When we examine the tests performed for each thrombocytopenia category, we notice that the majority of the tests had a positive yield of <20% and in some occasions 0%, even though the test was performed in over 60−70% of the study cohort. Some tests, like the ANA screen, had a higher percentage of positive results (18%) without any subsequent change in management, additional workup, or increased likelihood of receiving a rheumatologic diagnosis at follow-up. A similar pattern is seen with RF, which was tested in over 50% of the study cohort, with just 7% of these patients having a positive result; none of these patients had a subsequent change in management, likely due to lack of

Table 3. Logistic Regression Analysis Showing Associations of Development of Hematologic Malignancy and/or Explanation for the Thrombocytopenia at 1 year.

Variable	n/N (%)	Hematologic malignancy at 1 yr				Explanation for thrombocytopenia at 1 yr[a]			
		Univariate HR (95% CI)	p	Multivariate[b] HR (95% CI)	p	Univariate HR (95% CI)	p	Multivariate[b] HR (95% CI)	p
Severity of thrombocytopenia									
Severe (<50 k vs. 50−150 k)	36/472 (8)	2.08 (0.45−9.67)	0.35			3.66 (1.80−7.93)	<0.01		
Moderate/severe (<100 k vs. 100−150 k)[c]	171/472 (36)	2.41 (0.82−7.08)	0.11			2.53 (1.72−3.72)	<0.01	2.30 (1.52−3.48)	<0.01
Age (HR per 10-yr deciles)	n/a	1.46 (1.00−2.12)	0.05	1.52 (1.03−2.25)	0.03	1.02 (0.92−1.14)	0.69		
Sex (male vs. female)	282/472 (60)	1.71 (0.53−5.53)	0.37			0.91 (0.62−1.32)	0.60		
Concurrent anemia	130/472 (28)	1.48 (0.49−4.50)	0.49			1.62 (1.08−2.44)	0.02	1.28 (0.83−1.97)	0.26
Concurrent leukopenia	67/472 (14)	9.02 (3.02−26.91)	<0.01	9.97 (3.28−30.32)	<0.01	1.06 (0.62−1.78)	0.84		
Symptoms (mucosal bleeding, bruising)	84/472 (18)	1.27 (0.35−4.65)	0.72			1.68 (1.05−2.70)	0.03	1.17 (0.70−1.95)	0.54
Duration of thrombocytopenia (<1 yr vs. ≥ 1 yr)	169/472 (36)	1.00 (0.33−3.02)	0.99			1.05 (0.72−1.54)	0.81		

Note. CI = confidence interval; HR = hazard ratio. Bold font denotes significance in the multivariate model.

[a] Defined as a new diagnosis of hematologic malignancy, medication attributable effect, other hematologic diagnosis (e.g., Idiopathic thrombocytopenic purpura (ITP)), new solid cancer diagnosis, liver disease, rheumatologic disease, infection (e.g., HIV), nutritional deficiency, pregnancy, end-stage renal disease, spurious result (EDTA-clumping), or multiple of these.

[b] Forward selection method employed whereby any variable with $p < .10$ in univariate analysis was included in the multivariate model.

[c] For the multivariate models for "Explanation of Thrombocytopenia at 1 year," "Moderate/Severe" thrombocytopenia severity was used.

symptoms that could prompt further workup. Only one patient received a rheumatologic diagnosis at the 1-year follow-up mark (mixed connective tissue disease). Interestingly, this patient had significant fatigue and arthralgia in addition to mild thrombocytopenia, prompting further investigation for an underlying rheumatologic/autoimmune process.

Bone marrow biopsies were performed more often on patients with severe thrombocytopenia (64%) than on those with moderate (16%) and mild (8%) thrombocytopenia (Table 2). Of the patients with mild thrombocytopenia who had a bone marrow biopsy, five patients (21%) were diagnosed with a hematologic malignancy. Although this appears to be a high percentage for patients with mild reduction in platelet counts, all five patients had other concurrent hematologic abnormalities (anemia and/or leukopenia) or other clinically relevant symptoms that prompted the biopsy. Patients who had a bone marrow biopsy were also older (69 years vs. 61 years). Therefore, the procedure was directed at a high-risk subset of patients with mild thrombocytopenia and the high percentage of patients with a hematologic malignancy out of those who had bone marrow biopsies should not be generalized to all patients with mild thrombocytopenia.

As for infectious etiologies, testing for viral hepatitis was performed in 263 patients (50%) of our study population, and was able to detect four new cases of chronic viral hepatitis (B or C). Testing for HIV was performed in 37.5% of patients and was able to detect a single case of HIV. Despite the low yield of testing for infectious etiologies, these findings should not discourage providers from testing for viral hepatitis and HIV in patients with thrombocytopenia, especially as the Centers for Disease Control and Prevention (CDC) recommends routine screening for HIV infection for all patients aged 13−64 years [7], and routine screening for all patients born between 1945 and 1965 or those with risk factors for hepatitis C virus [8].

Referral to a hematologist is appropriate to confirm any new diagnosis in a patient with thrombocytopenia or to determine the cause of any unexplained thrombocytopenia, especially in cases of moderate to severe thrombocytopenia. Hematology referrals for asymptomatic mild thrombocytopenia have always been an area of debate; some studies have shown that as low as 3% of these patients required an intervention by a hematologist and normalization of platelet counts within 1 month in patients with normal bleeding history and no positive physical examination findings [9]. Another study showed that 11% of patients normalized their platelet counts, <1% developed a hematologic

Table 4. Other Hematologic Abnormalities, Signs, or Symptoms in Patients with New Hematologic Malignancy.

Patient	Thrombocytopenia severity at presentation	Symptoms and signs	Other laboratory abnormalities
CLL/SLL − 1	Mild	Night sweats and lymphadenopathy	Leukocytosis/lymphocytosis
CLL/SLL − 2	Mild	None	Leukocytosis/lymphocytosis
CLL/SLL − 3	Moderate	None	Leukocytosis/lymphocytosis
CLL/SLL − 4	Moderate	Splenomegaly	Leukocytosis/lymphocytosis
Chronic myelomonocytic leukemia	Moderate	Bruising, splenomegaly	Anemia, leukopenia
LGL leukemia − 1	Severe	Mucosal bleeding	Leukopenia
LGL leukemia − 2	Moderate	None	Leukopenia
Low-grade B-cell lymphoma	Moderate	None	Leukopenia
Marginal zone lymphoma	Mild	30 lbs. weight loss	None
Myelodysplastic syndrome − 1	Mild	None	Anemia, leukopenia
Myelodysplastic syndrome − 2	Moderate	None	Anemia, leukopenia
Multiple myeloma − 1	Mild	None	Anemia, leukopenia
Multiple myeloma − 2	Mild	None	Leukopenia
T-ALL	Severe	Constitutional symptoms	Anemia, leukopenia

Note. CBC = complete blood count; CLL/SLL = chronic lymphocytic leukemia/small lymphocytic lymphoma; HIV = human immuno-deficiency virus; LFT = liver function test; LGL = large granular lymphocytic leukemia; T-ALL = T-cell acute lymphoblastic leukemia.

malignancy or an autoimmune disorder, and the majority (88%) had stable platelet counts during the 6-month monitoring period. Interestingly, a 12% 10-year probability of developing an autoimmune disease (other than immune thrombocytopenic purpura) was noted [10].

Our study also supports the need for a cost-effective analysis for patients with thrombocytopenia given the low yield and high cost for most tests ordered for these patients. Although such studies are limited given the broad population and the variety of tests ordered, cost-effective analyses have been performed in populations who had specific tests for specific disorders (e.g., HIT antibodies for heparin-induced thrombocytopenia) [11,12]. These studies reached conclusions consistent with our findings: an approach of informed testing guided by signs, symptoms, and laboratory findings and based on pre-test probability is preferred to a gunshot approach in low-risk populations.

We acknowledge that there are several limitations to our study, the first being the retrospective nature of the analysis. In addition, our study examines a racially diverse urban city population [13], where environmental, socioeconomic, and ethnic factors could have a potential influence on the etiology or even normal variation in platelet counts. The study population is also skewed towards a cohort with
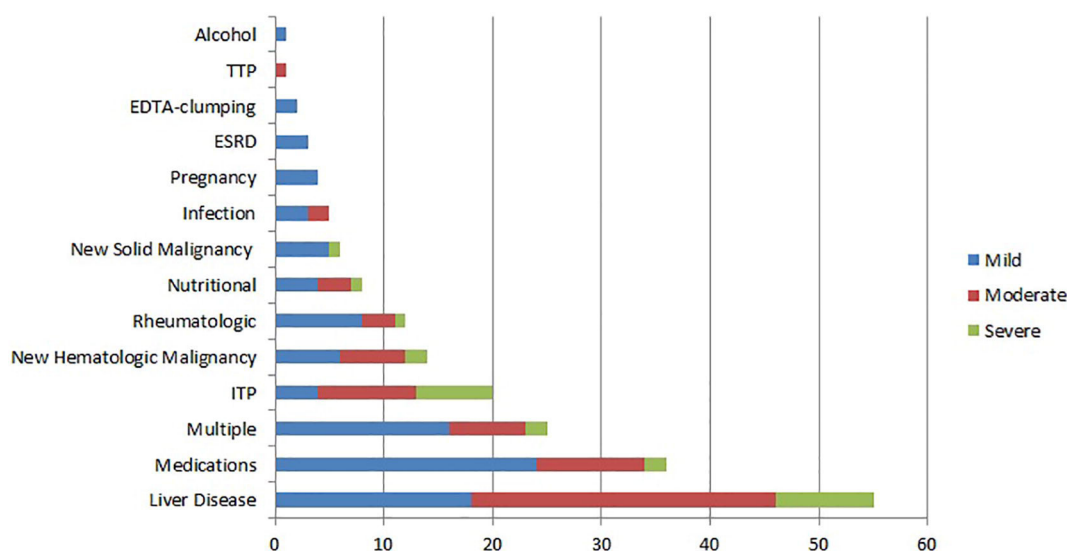

Fig. 1. Confirmed/plausible explanations of thrombocytopenia at 1 year in 192/472 patients (40.7%) with degree of thrombocytopenia at presentation. Note. ESRD = end-stage renal disease; ITP = idiopathic thrombocytopenic purpura; TTP = thrombotic thrombocytopenic purpura. There was no clear explanation for thrombocytopenia at 1 year in 280/472 patients (59.3%; not shown in this figure).

higher rates of alcohol abuse and chronic alcoholic or viral liver disease (14.4% vs. 1.8% for the general US population) [14], as the study was conducted in a major liver transplant center. All these factors can have a significant effect on the various etiologies of thrombocytopenia in our study compared with populations in different geographical regions across the country. Finally, the workup was subject to decisions of individual hematologists and not standardized for the 472 patients, leaving the possibility that some potential diagnoses were undetected. Furthermore, several clonal disorders have recently been recognized and described, but these require laboratory testing platforms that had not been implemented during the study period (i.e., clonal hematopoiesis of unknown significance [CHIP], clonal cytopenia of undetermined significance [CCUS], and idiopathic cytopenia of undetermined significance [ICUS]).

In conclusion, thrombocytopenia is a frequent laboratory finding prompting referral to hematology subspecialty clinics. Outcomes of patients with thrombocytopenia vary based on severity with a higher likelihood of finding a putative explanation at 1 year in patients with moderate to severe thrombocytopenia. Concurrent leukopenia and increasing age were independently associated with higher relative odds of being diagnosed with a hematologic malignancy at 1 year. Lastly, in asymptomatic patients with mild thrombocytopenia, laboratory testing did not reveal any major positive findings and patients did not develop any significant hematologic, infectious, or rheumatologic disorders within 1 year of follow-up. Our study also demonstrates the need for an algorithmic evidence-based approach for referral and testing for thrombocytopenia.

Authors' contributions

Zaid Abdel Rahman: study design, collection and analysis of data. Yaser Alkhatib and Vijaya Donthireddy: study design. Hiba Jabbour: data collection. Kevin Miller: data analysis. All authors participated in writing the paper and approved the final version

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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