



Prevalence of Heparin-Induced Thrombocytopenia Type II among Cardiac Surgery Patients

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Abstract

Objective: To assess the prevalence of heparin - induced thrombocytopenia type II (HIT) among suspected patients who received heparin in cardiac surgery intensive care unit at a single tertiary care hospital.

Method: This is a retrospective cohort study conducted to calculate the prevalence of HIT type II among all patients who underwent cardiac surgery and tested for HIT over one decade, from 1st of January 2004 to 31st of December 2014. Patients who were suspected to have HIT were stratified according to the results of HIT assay result, using Diamed PaGIA and/or ELISA screening test, into two groups; HIT positive group and HIT negative group.

Result: During the study period, 5,104 patients had cardiac surgery, 264 patients were suspected clinically to have HIT with a prevalence of 5.17% (95% CI, 4.59% to 5.81%). Out of these patients only 35 patients had positive test result, with a prevalence of 13.25% (95% CI, 9.11% to 17.28%). This makes the prevalence among the whole population to be 0.68% (95% CI, 0.45% to 0.91%). In the 264 cases of suspected HIT, the retrospectively calculated 4T's probability score were high among 30 patients (11.4%), intermediate in 197 (74.6%) and low in 37 patients (14%). Among HIT negative patients there was a significant difference between risk of developing thrombocytopenia and selected pre-defined confounding variables; particularly sepsis and the use of cardiac devices (P value <0.001).

Conclusion: The prevalence of true HIT type II among cardiac patients is rare, although it's not uncommon among clinically suspected cases.

Keywords: Heparin-induced thrombocytopenia; Low molecular weight heparin; CSICU

Abbreviations

CSICU: Cardiac Surgery Intensive Care Unit; CT: Computed Tomography; ECMO: Extracorporeal Membrane Oxygenation; ELISA: Enzyme Immune Assay Test; IABP: Intra-Aortic Balloon Pump; HIT: Heparin-Induced Thrombocytopenia Type II; Hg: Hemoglobin; KFSH&RC: King Faisal Specialist Hospital and Research Centre; LMWH: Low Molecular Weight Heparin; MR: Magnetic Resonance; SRA: Serotonin Release Assay; UFH: Unfractionated Heparin; VAD: Ventricular Assist Device

Background

There are two types of heparin-induced thrombocytopenia (HIT). Heparin-induced thrombocytopenia type I that occurs in 10% to 20% of patients receiving heparin [1], and HIT type II that occurs between the fifth and fourteenth day of heparin therapy unless there was a previous heparin exposure. Type II HIT is one of the serious side-effects associated with heparin therapy [2].

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The incidence of HIT type II has been reported to range from 1% to 5% among patients using heparin [1], and is more commonly seen in orthopedic surgery patients receiving UHF [3]. Early diagnosis of HIT type II is crucial to prevent thrombosis complications. Despite the relatively high prevalence of anti-PF4/heparin antibodies in patients undergoing cardiac surgery, the incidence of HIT in this patient population is about 2.4% [3].

Laboratory analysis should be done to confirm the diagnosis of suspected HIT for all cases associated with intermediate or high probability of HIT type II as defined by the 4T's probability score which consist of thrombocytopenia, time of thrombocytopenia, thrombosis, and absence of other causes of thrombocytopenia [2,4]. However, there are some inconsistencies when it comes to the definition of suspected HIT and HIT type II [5-10]. Regardless, HIT type II is defined as unexplained thrombocytopenia, with a 30% to 50% reduction of the platelet from baseline occurring within 5-14 days after initiating heparin with or without thrombosis in addition to the positive gold standard assay; serotonin release assay "SRA" [11]. Others defined diagnosis of HIT type II depends on screening tests (Diamd gel or ELISA) and functional assay (SRT). The sensitivity and specificity of these tests are different and affect the rate of HIT diagnosis.

For patients who are receiving UFH, there are various factors that can lead to thrombocytopenia other than UFH itself, which may complicate the diagnosis and management. Incorrect diagnosis or high suspicious of HIT may lead many practitioners to initiate HIT management. In cardiac surgery intensive care unit (CSICU), several other factors including drug-induced thrombocytopenia, surgery and sepsis [12,13], can further complicate the diagnosis. Therefore, we hypothesize that the prevalence of HIT type II is overestimated among suspected cases who received UFH or Low Molecular Weight Heparin (LMWH) which may lead to inappropriate management sequel. This study aims to assess the prevalence of HIT type II among suspected patients who received UHF or LMWH in post-cardiac surgery patients. Additionally, the study will assess the performance of 4T's probability scoring in retrospective manor whenever it is possible in the same setting.

Methods

Study design

This is a retrospective cohort study that aims to assess the prevalence of HIT type II among all cases of suspected HIT in CSICU and its step down units. All patients who were admitted to CSICU in our institution and transferred to one of its step down units over one decade, from 1st of January 2004 to 31st of December 2014 were included in the study. Patients who were clinically suspected for HIT were stratified according to the result of the HIT assay into group A "patients who had positive HIT test" and group B "patients who had negative for HIT test", and then were compared with regard to clinical presentation and management consequences. Suspected HIT was defined as all cases who had HIT assay test positive for enzyme immune assay test "ELISA" and/or "Diamed PaGIA" test during the study period. Where, HIT type II was defined as all cases that had a positive HIT assay result.

Study population

All patients who were suspected to have HIT during the defined study period, at CSICU and its step down units at King Faisal Specialist Hospital and Research Centre (KFSH & RC), Riyadh, Saudi

Arabia, were included.

Inclusion criteria

All adult and pediatric patients who were admitted to CSICU and its step down units with suspected HIT were included in the study. The study was approved by the Research Advisory Council (RAC: 2151029).

Data collection

The medical charts of all suspected patients as defined previously, from 2004 through 2014, were reviewed, and the following data were collected: demographic data, drug data (history of using UFH\LMWH, within the last three months, type of non-heparin anticoagulant used for suspected HIT, including lepirudin, bivalirudin, argatroban or fondaparinux), laboratory data (baseline platelet count, nadir platelet count, follow up platelet count for 14 days [14] after sending HIT assay, baseline hemoglobin (Hg), fibrinogen, and D - dimer level), 4T's score at time of suspected HIT, result of HIT assay, chart documentation of confirmed HIT, and other clinical outcomes including documentation of radiologically confirmed venous/arterial thromboembolism, and major bleeding that is defined as clinical evidence of bleeding documented in patients' chart with therapeutic intervention including blood product and/or pharmacological agents administration, ICU mortality, and hospital length of stay. Also we assessed the presence or absence of other confounding factors defined as sepsis, cardiac surgery; type of cardiac surgery; drug-induced thrombocytopenia including GP II(b)/III(a) inhibitor, amiodarone, carbamazepine, milirirone, valproic acid, phenytoin and cardiac devices used such as intra-aortic balloon pump (IABP), extracorporeal membrane oxygenation (ECMO) and ventricular assist devices (VADs).

Outcome measures

The primary outcome of our study was to assess the prevalence of HIT type II among cardiac surgery patients with suspected HIT. Several secondary outcomes were measured including; the 4T's probability scoring which consist of thrombocytopenia, time of thrombocytopenia, thrombosis, and absence of other causes of thrombocytopenia at the time of suspecting HIT, the correlation between high, moderate, and low clinical probability using 4T's scoring and the presence of HIT type II, impact of overall use of non-heparin anticoagulants and the suspicion of HIT in terms of presence of thrombosis and length of hospitalization among all suspected cases comparing group A (positive HIT test) to group B (negative HIT test). Impact of overall use of non-heparin anticoagulants in terms of major bleeding during and after their use among all suspected cases and comparing group A with group B for the rate of discontinuation of non-heparin anticoagulants and re-initiation of heparin among patients who had negative HIT assay results, electronic chart documentation and time of platelet recovery among all suspected cases and comparing group A and group B. The correlation between thrombocytopenia and the presence of one of the confounding factors; drug-induced thrombocytopenia, sepsis, type of cardiac surgery, and the use of cardiac devices were assessed. The predictive value of using 4T's among cardiac surgery patients, and the correlation between age and risk of developing thrombocytopenia, as well as correlation between age and results of negative HIT assay were also investigated.

Statistical analysis

Taking into account the data previously reported [15], we hypothesized that the incidence of HIT among suspected cases will

Table 1: Baseline characteristics of all patients with suspected Heparin-induced Thrombocytopenia (HIT) type II.

Variables	All patients (n=264)
Adult Age	
Age in year, (Mean ± SD)	50 ± 17
Pediatric Age	
Age in year, (Mean ± SD)	1 ± 3
Gender of 264 patients	
Male, n (%)	131 (49.62)
Female, n (%)	133 (50.38)
Number of days staying in the hospital	
Medical unit, (Mean days ± SD)	57.6 ± 66.9
Past cardiovascular medical history, n= 264	
Coronary artery disease, n (%)	66 (25)
Valvular heart disease, n (%)	115 (43.6)
Heart failure, n (%)	42 (16)
Congenital heart disease	89 (33)
Atrial fibrillation, n (%)	19 (7.2)
Peripheral artery disease, n (%)	10 (3.8)
Others, n (%)	49 (18.6)
Invasive interventions for 260 patients*, n= 260	
On pump procedure, n (%)	213 (91.4)
Cardio-pulmonary bypass time in minutes, (mean ± SD)	145 ± 72.9
Aortic cross-clamping time in minutes, (mean ± SD)	92.7 ± 64.4
Off-pump procedure	20 (8.6)
Type of procedures*, n= 260	
Coronary artery bypass grafting, n (%)	45 (17.3)
Valvular heart surgery, n (%)	114 (43.8)
Cardiac catheterization, n (%)	4 (1.5)
Congenital heart disease correction, n (%)	60 (23)
Heart transplant, n (%)	18 (6.9)
Left ventricular assist device insertion, n (%)	3 (1.1)
Right ventricular assist device insertion, n (%)	9 (3.5)
Biventricular assist device insertion, n (%)	1 (0.4)
Extracorporeal membrane oxygenation, n (%)	70 (30)
Vascular surgery, n (%)	16 (6.1)
Others, n (%)	1 (0.4)

*Analysis done for 260 patients, as four patients admitted to Cardiac Surgery Intensive Care Unit (CSICU) but they did not undergo any invasive/surgical interventions.

be around 0.47% among surgical ICU patients and 27% among suspected cases admitted to cardiac surgery ICU. From a brief review of charts, it was projected that approximately 350 patients will qualify as HIT type II suspected cases. If the incidence of true HIT type II is as high as 27%, then the true incidence should be estimated to be within five percentage points. Continuous variables were expressed as the mean + SD and categorical variables as percentages. For categorical variables, comparisons were made using the χ^2 test or Fisher exact test and continuous variables was made using the student t-test. We compared the two groups by using a student t-test. For those variables which showed non-normality on the distribution, the non-parametric Wilcoxon test was used instead. Multivariable analysis was used in

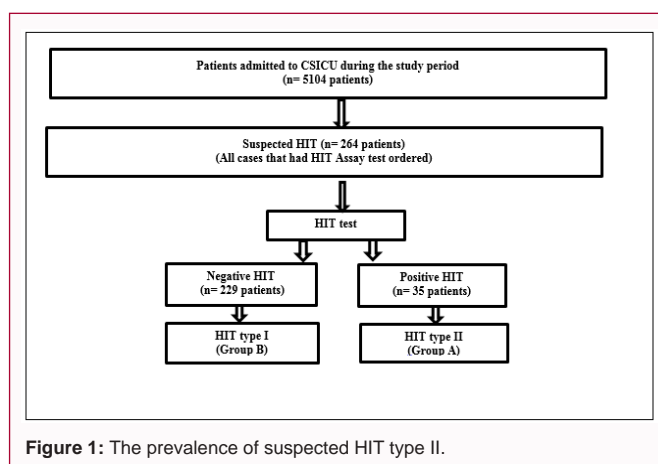


Figure 1: The prevalence of suspected HIT type II.

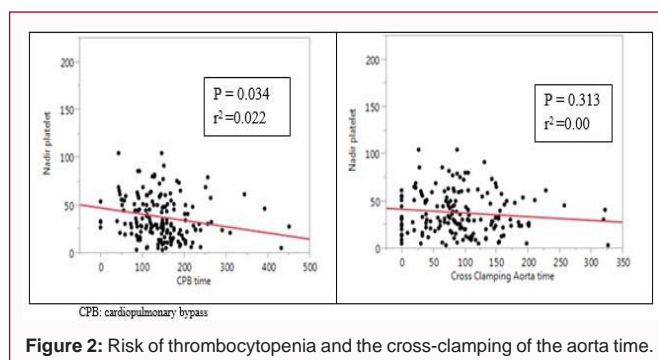


Figure 2: Risk of thrombocytopenia and the cross-clamping of the aorta time.

the situation where more than one independent factor was analyzed for one outcome at the same time. SAS version 9.4 software was used to analyze the data.

Results

During the study period, 5104 patients had cardiac surgery, from those 264 patients were clinically suspected to have HIT. Details of baseline characteristics of all 264 subjects, with comparison for both groups, are presented in (Table 1) and Table 2. The prevalence of suspected HIT type II was 5.17% (95% CI, 4.59% - 5.81%), (Figure 1). Based on the results of Diamed PaGIA and or ELISA screening test we found that only 35 patients tested positive for one or more of the HIT tests, with a prevalence of 13.25% (95% CI, 9.11% - 17.28%) among the suspected HIT, and 0.68% (95% CI, 0.45% - 0.91%) among the whole study population. Among the 264 cases of suspected HIT, the calculated 4T's probability score were high among 30 patients (11.4%), intermediate in 197 (74.6%) and low in 37 patients (14%). Moreover, among those who had a positive HIT assay the "high" 4T's probability score encountered in one patient only (2.8%), "intermediate" encountered in 29 (82.86%), and "low" encountered in 5 patients (14.3%). The "intermediate" and "high" 4T's scores have a sensitivity of 85.7% (95% CI, 0.49% - 1.23%) and a specificity of 14% (95% CI, 0.095% - 0.185%) in predicting true HIT among cardiac surgery patients with suspected HIT. The positive predictive value of 4T's scoring was 13.2% (95% CI, 0.088% - 0.176%), and negative predictive value 86.5% (95% CI, 0.753% - 0.974%).

We found that there were no differences in the baseline hematological values and other label parameters between the positive HIT patients compared to negative HIT patients, (Table 2). Also, we found no difference between HIT positive patients and HIT negative patients in regard to the distribution of confounding factors, that

Table 2: Baseline characteristics among suspected Heparin-induced Thrombocytopenia (HIT) stratified based on HIT test results.

Variables	Positive HIT (n = 35)	Negative HIT (n = 229)	P value
Adult age			
Age in year, (Mean)	50.041	50.23	0.939
Pediatric age			
Age in year, (Mean)	0.4065	1.494	0.501
Gender			
Male, n (%)	14 (40)	117 (51)	0.223
Female, n (%)	21 (60)	112 (49)	
Number of days staying in the hospital			
Medical unit, (Mean days \pm SD)	59.9 \pm 84	57.2 \pm 64.1	0.86
Past cardiovascular medical history			
Coronary artery disease, n (%)	14 (40)	52 (22.7)	0.028
Valvular heart disease, n (%)	20 (57)	95 (41.5)	0.0819
Heart failure, n (%)	6 (17.14)	36 (15.7)	0.8303
Congenital heart disease	3 (8.6)	86 (37.5)	0.0007
Atrial fibrillation, n (%)	4 (11.4)	15 (6.5)	0.2935
Peripheral artery disease, n (%)	zero	10 (4.36)	0.368
Invasive interventions, n= 260s			
On pump procedure, n (%)	28 (80)	188 (82.1)	0.765
Cardio - pulmonary bypass time in minutes, (mean \pm SD)	158.4 \pm 83.7	143.1 \pm 71.1	0.39
Aortic cross-clamping time in minutes, (mean \pm SD)	94.2 \pm 67.7	92.5 \pm 64.0	0.91
Off-pump procedure	2 (5.7)	18 (7.9)	0.713
Type of procedures, n= 260			
Coronary artery bypass grafting, n (%)	10 (28.6)	35 (15.3)	0.0515
Valvular heart surgery, n (%)	20 (57.1)	94 (41)	0.0734
Cardiac catheterization, n (%)	1 (2.8)	3 (1.3)	0.5222
Congenital heart disease correction, n (%)	2 (5.7)	58 (25.3)	0.0085
Heart transplant, n (%)	zero	18 (7.86)	0.142
Left ventricular assist device insertion, n (%)	zero	3 (1.31)	0.988
Right ventricular assist device insertion, n (%)	2 (5.7)	7 (3)	0.988
Biventricular assist device insertion, n (%)	zero	zero
Extracorporeal membrane oxygenation, n (%)	6 (17.1)	64 (28)	0.6833
Vascular surgery, n (%)	4 (11.4)	12 (5.24)	0.153
Others, n (%)	zero	1 (0.4)	0.988

There is a significant different between Heparin-induced Thrombocytopenia (HIT) positive group and HIT negative group, P value <0.05.

might influenced the development of HIT type II, (Table 3).

Among the 264 patients of suspected HIT, thrombosis developed in 16 patients (6.1%); 15 (6.55%) of them had negative HIT and one patient (2.87%) had positive HIT; p-value=0.44. Among the 264 patients with suspected HIT, non-heparin anticoagulants were used in only 13 patients (4.92%), and there was no difference in the development of thrombosis among patients who used non-heparin anticoagulant compared to those who were kept on heparin. On the other hand, among the suspected HIT patients bleeding developed in 100 patients (37.9%), 20 patients (20%) had positive HIT test. Where all of them received blood product, but platelet transfusion was given for 18 patients (18%), while surgical interventions were done for 13 of them (13%), and 24 patients (24%) received pharmacological agents to reverse bleeding. From those 100 patients who developed bleeding, 20 patients (20%) had positive HIT test and all of them received

blood transfusions, and 3 (15%) of them received platelet transfusion. Moreover, there was no significant difference in the hospital stay, and mortality among non-heparin anticoagulant users in those with HIT positive (3 patients) and HIT negative patients (10 patients) who did not use non-heparin anticoagulants. Also there was no difference in the hospital stay and mortality between those with HIT positive and HIT negative in general despite using non-heparin anticoagulant, which can be hard to interpret because of the small sample size. Electronic chart documentation for the result of positive HIT was done only for 21 (60%) patients out of 35 patients.

One-way analysis revealed that among HIT negative patients there was a significant difference between risk of developing thrombocytopenia and the pre-defined confounding variables; sepsis and the use of cardiac devices; with P value < 0.001. Moreover, the mean reduction in platelet count was higher among negative HIT

Table 3: Laboratory variables for all patients of suspected Heparin-induced Thrombocytopenia (HIT); comparing HIT positive to HIT negative patients.

Variables	All patients (n = 264)	Positive HIT (n = 35)	Negative HIT (n = 229)	P value
Laboratory variables				
Baseline platelet, (Mean ± SD)	225.2 ± 114.2	205.1 ± 88.1	228.2 ± 117.6	0.17
Nadir Platelet, (Mean ± SD)	41 ± 30	47.2 ± 31.5	39.9 ± 28.5	0.20
Platelet reduction, ((Mean ± SD)	81.7 ± 073.73	77 ± 64.24	82.51 ± 75.8	0.56
Platelet count when HIT test was sent, (Mean ± SD)	62.3 ± 46.7	75.2 ± 70.2	60.3 ± 41.9	0.23
Baseline Partial thromboplastin time in seconds, (Mean ± SD)	45.8 ± 21.7	44.2 ± 16.4	46.1 ± 22.4	0.55
Partial thromboplastin time when HIT test was sent, (Mean ± SD)	62.8 ± 27	60.6 ± 24	63.2 ± 27.5	0.56
Baseline Hemoglobin level, mg/dL (mean ± SD)	120.4 ± 24.5	111.5 ± 25.1	121.8 ± 24.2	0.028
WBC count, 10 ⁹ /L	13.5 ± 9.8	13.5 ± 7.8	13.5 ± 10.1	0.997
Band cell	6.1 ± 6.7	4.44 ± 5.4	6.4 ± 6.9	0.075
Fibrinogen level, g/L (Mean ± SD)	2.7 ± 1.5	2.8 ± 1.7	2.6 ± 1.5	0.33
D-Dimer level, (Mean ± SD)	2090.5 ± 3355	2367.6 ± 4587.8	2050.9 ± 3175.1	0.821
C-reactive protein, mg/L, (mean ± SD)	55.5 ± 74.5	35.1 ± 34.1	59.1 ± 79	0.209
Procalcitonin, (Mean ± SD)	20.1 ± 53.4	8.3 ± 13.14	22.1 ± 57.1	0.153
Blood Glucose level, mmol/L, (mean ± SD)	7.6 ± 2.3	8.2 ± 2.7	7.5 ± 2.2	0.21
Body Temperature, (mean ± SD)	36.7 ± 0.64	36.7 ± 0.59	36.7 ± 0.66	0.824

There is a significant different between HIT positive group and HIT negative group, P value <0.05.

Table 4: Distribution of confounding factors among all patients with suspected HIT; comparing HIT positive to HIT negative patients.

Variables	All patients (n = 264)	Positive HIT (n = 35)	Negative HIT (n = 229)	P value
Sepsis [†]	120 (45.4)	15 (42.9)	105 (87.5)	0.7404
Presence of external device, n (%)	55 (20.3)	8 (22.9)	47(85.45)	0.7516
Use of drug associated with thrombocytopenia [#] , n (%)	114 (43.2)	18 (15.7)	96 (84.2)	0.2903
Positive for confounding variables [§] , n (%)	179 (67.8)	26 (74.3)	153 (85.4)	0.378
Types of heparin used, n= 218				
Unfractionated heparin, n (%)	167 (80.3)	23 (65.7)	144 (86.2)	0.746
Low molecular weight heparin, n (%)	49 (23.5)	5 (14.3)	44 (89.8)	0.4849
History of using heparin in the last 100 days, n (%)	43 (16.3)	6 (17)	37 (86)	0.883
Indications of heparins				
As treatment, n (%)	12 (5.8)	3 (8.6)	9 (3.9)	0.2025
As prophylaxis, n (%)	196 (94.2)	26 (74.3)	184 (80.3)	0.322
Percentage of heparin discontinuation	103 (49.5)	14 (40)	89 (38.9)	0.898
Percentage of heparin re-initiation	69 (33.2)	5 (14.3)	64 (27.9)	0.0867

[†]Sepsis: defined as an infection together with systemic manifestations of infection including: fever temperature >38.3°C, hypothermia temperature <36°C, heart rate >90/min⁻¹, tachypnea, hyperglycaemia (plasma glucose > 140 mg/dL or 7.7 mmol/L) in the absence of diabetes, leukocytosis (WBC count >12,000 μL⁻¹), leukopenia (WBC count <4000 μL⁻¹), normal WBC count with greater than 10% immature forms, plasma C-reactive protein more than two SD above the normal value or Plasma procalcitonin more than two SD above the normal value⁴.

[#]Drugs induced thrombocytopenia that we looked at are: Glycoprotein II(b)/III(a) inhibitor, Amiodarone, Carbamazepine, Valproic acid, Phenytoin.

[§]confounding variables includes 114 patient used drug-induced thrombocytopenia, 120 developed sepsis and 54 had an external cardiac device.

patients who had ECMO -87.816 + 3.72, and patients who had IABP -82.780 + 4.31 compared to negative HIT who had not have cardiac device not -76.286 + 1.33, and -77.099 + 1.33, P value < 0.05. The type of surgery did not influence the risk of thrombocytopenia (Table 4).

In patients who had on-pump surgery, there was a positive correlation between thrombocytopenia and the prolonged time of cardiopulmonary bypass, while no influence on the risk of thrombocytopenia and the cross-clamping of the aorta time, Figure 2.

Young patients, who have mean age under 30.7 + 19.8 years, were more susceptible to develop thrombocytopenia than patients whose

age was more than 45.3 + 31 years, with P value 0.0001. Reversibly, we found that the risk of getting HIT positive is significantly higher among older patients; median age for positive HIT was 52.32 years (IQR, 35.4 - 60) versus 37.2 years (IQR, 0.88 - 56.9), P value 0.0096.

Discussion

In our study we found that the prevalence of HIT type II to be low, 0.68%, among cardiac surgery patients. This prevalence falls in the range of previously published studies that ranged between 0.2% - 1.4%. However, we had a great interest to know the prevalence of HIT type II among the suspected cases, and we found it to be 13.2%,

which means one patient of every eight suspected cases will have true HIT type II. This consistent finding will help in understanding that there are many factors that could contribute to the development of thrombocytopenia among patients post-cardiac surgery. Also these factors could affect the decision of using non-heparin anticoagulant among suspected cases [16].

As it is known, 4T's scoring system is validated to identify patients with low, intermediate or high probability of HIT type II, as a screening tool before sending the confirmatory test. Moreover, it is well established that 4T's probability scoring system have high sensitivity with inconsistent specificity for HIT type II. In general, patients with intermediate or high 4T's probability have a sensitivity range between 89% and 100% and specificity range between 39% and 76%. Our study showed a sensitivity of 85.7% and specificity of 14%, only. This can be explained by the multi-factorial causes of thrombocytopenia in this setting. Therefore, 4T's probability scoring system has a high negative predictive value for HIT type II, and negligible positive predictive value among cardiac surgery patients suspected to have HIT type II. It's very well known that some confounding factors may contribute to the development of thrombocytopenia in cardiac surgery patients apart from heparin; some of these factors have valuable size on the impact of 4 T's probability. In our study we found that the risk of thrombocytopenia higher among patients who have these confounding factors. Moreover, there was no difference in the development of thrombosis and bleeding among HIT positive and HIT negative patients. Using non-heparin anticoagulant did not influence the duration of hospital stay, this can be attributed to its use in small percentage of suspected cases of HIT type II. Additionally, we detected a significant risk of developing thrombocytopenia in patients with sepsis and patients who had ECMO or IABP [17]. Furthermore, there is positive correlation between the development of thrombocytopenia and the cardiopulmonary bypass time. The present findings of the positive association between thrombocytopenia and mechanical cardiac assist devices reaffirm that they should be considered while diagnosing HIT type II among cardiac surgery patients who were placed on these devices. Furthermore, it flags the importance of re-validating and revising the 4T's probability score if it will be used in cardiac surgery setting. Providing the predictive value for the clinical probability score and highlighting the effect of confounding factors on the development of thrombocytopenia in cardiac surgery setting; a prospective clinical study using specific clinical probability score for cardiac surgery patients is warranted. Our study has some limitations, including the retrospective design. There was incomplete information about the total amount of platelet transfusion received and the amount of platelets used among thrombocytopenic patients.

Conclusion

The prevalence of true HIT type II among cardiac patients is rare, although it's not uncommon among suspected cases. The use of 4T portability scoring in this setting demonstrated high sensitivity, but low specificity may be due to the multi-factorial cause of thrombocytopenia.

References

1. Cleveland KW. Argatroban: A New Treatment Option for Heparin-Induced Thrombocytopenia. *American Association of Critical-Care Nurses*. 2003;23:61-66.
2. JTVMA Hall. Heparin-induced thrombocytopenia in the intensive care unit: Review articles. *The Intensive Care Society*. 2010:20-5.
3. Girolami A, Girolami B. Heparin-induced thrombocytopenia: a review. *Semin Thromb Hemost*. 2006;32(8):803-9.
4. Lo GK, Juhl D, Warkentin TE, Sigouin CS, Eichler P, Greinacher A. Evaluation of pretest clinical score (4 T's) for the diagnosis of heparin-induced thrombocytopenia in two clinical settings. *J Thromb and Haemost*. 2006;4(4):759-65.
5. Franchini M. Heparin-induced thrombocytopenia: an update. *Thrombosis Journal* 2005;3(14):1-5.
6. Kasirajan K. Outcomes after heparin-induced thrombocytopenia in patients with Propaten vascular graft (Abstract). *Ann Vasc Surg*. 2012;26(6):802-8.
7. Almeida JI, Coats R, Liem TK, Silver D. Reduced morbidity and mortality rates of the heparin-induced thrombocytopenia syndrom (abstract). *J Vasc Surg*. 1998;27(2):315-6.
8. Trehel-Tursis V, Louvain-Quintard V, Zarrouki Y, Imbert A, Doubine S, Stéphan F, et al. Clinical and Biologic Features of Patients Suspected or Confirmed to Have Heparin-Induced Thrombocytopenia in a Cardiothoracic Surgical ICU. *CHEST*. 2012;142(4):837-44.
9. Levy JH, Winkler AM. Heparin-induced thrombocytopenia and cardiac surgery. *Curr Opin Anaesthesiol*. 2010;23(1):74-9.
10. Smythe MA, Koerber JM, Mattson JC. The Incidence of Recognized Heparin-Induced Thrombocytopenia in a Large, Tertiary Care Teaching Hospital. *CHEST*. 2007;131:1644-9.
11. Bakchoul T, Greinacher A. Recent advances in the diagnosis and treatment of heparin-induced thrombocytopenia. *Ther Adv Hematol*. 2012;3(4):237-51.
12. Greinacher A. Heparin-Induced Thrombocytopenia. *N Engl J Med*. 2015;373:252-61.
13. Ortel TL. Heparin-induced thrombocytopenia: when a low platelet count is a mandate for anticoagulation. *Hematology Am Soc Hematol Educ Program*. 2009:225-32.
14. Keeling D, Davidson S, Watson H, Keeling D. The management of heparin-induced thrombocytopenia. *Br J Haematol*. 2006;133(3):259-69.
15. Harris M, Taylor G. *Medical Statistics Made Easy*. United States of America: Springer-Verlag New York Inc. 2003.
16. Laber DA, Martin ME. Etiology of thrombocytopenia in all patients treated with heparin products. *Eur J Haematol*. 2005;75(2):101-5.
17. So Yeon Lim, Eun Ju Jeon, Hee-Jin Kim, Kyeongman Jeon, Sang-Won Um, Won-Jung Koh, et al. So Yeon Lim. The Incidence, Causes, and Prognostic Significance of New-Onset Thrombocytopenia in Intensive Care Units: A Prospective Cohort Study in a Korean Hospital. *Emergency & Critical Care Medicine*. 2012;27(11):1418-23.