Original Article

Underutilization of pharmacological thromboprophylaxis in obstetrics and gynaecology patients in the absence of a risk assessment tool

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Abstract

Objective: This study was conducted to determine the risk factors for developing venous thromboembolism and to evaluate adherence to thromboprophylaxis guidelines among patients hospitalized in Obstetrics and Gynaecology units.

Methods: A retrospective cohort study was conducted from December 2015 to March 2016 in the haematology department of a teaching hospital. A total of 188 hospitalized female patients with a hospital length of stay greater than 1 day were included. Patient data were reviewed to assess the risk score for developing venous thromboembolism by an independent expert haematologist. Patients eligible for thromboprophylaxis were compared to patients who had already received thromboprophylaxis.

Results: A total of 188 patients were included, with age ranging from 17 to 81 years. Of these, 61% percent (n = 116) were gynaecological patients, while the remainder were pregnant women admitted to the obstetrics ward (38%, n = 72). Based on independent expert decision, 54% of gynaecological patients and 37% of obstetrics patients were eligible for thromboprophylaxis; however, only 48% of gynaecological and 26% of obstetrics patients were given thromboprophylaxis by their treating physician.

Conclusions: Venous thromboembolism is associated with substantial mortality and is largely preventable. Our study reports underutilization of thromboprophylaxis in clinical practice. Different modalities are necessary to improve adherence to thromboprophylaxis, such as

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implementation of a risk stratification tool at the time of hospital admission.

**Keywords:** Pregnant and non-pregnant women; Risk assessment tools; Thromboprophylaxis and venous thromboembolism

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**Introduction**

Venous thromboembolism (VTE), consisting of deep vein thrombosis (DVT) and pulmonary embolism (PE), is a common disease that occurs with an incidence of approximately 1 per 1000 annually in adult populations. The incidence rate approaches 5–6 per 1000 annually by age 35. The major outcomes of venous thrombosis are death, recurrent DVT and post-thrombotic syndrome. There are also differences in the incidence of diagnosed venous thrombosis among ethnic groups with lower rates, in the United States, in Asians, Pacific Islanders and Hispanics than in whites.

VTE is of multifactorial origin, and understanding of the risk factors is necessary to maximize the prevention of this disease in high risk patients. The major risk factors for thrombosis include surgery, hospitalization, immobility, trauma, cancer, obesity, pregnancy, the puerperium, hormone use, cancer, obesity, or inherited and acquired disorders of hypercoagulation. A study followed 21,680 persons for of VTE occurrence over 7.6 years in the general population. The most common factors were hospitalization in 52%, cancer in 48% and surgery in 42%, revealing that VTE can be avoided with the proper prophylaxis in these setting. This highlights the tremendous potential that thromboprophylaxis might have if were administered optimally in at risk patients. VTE risk assessment and thromboprophylaxis for high risk groups can help minimize PE related mortality.

Overall, the age-adjusted annual incidence rate of VTE is higher for men than for women; however, the incidence rates are somewhat higher in women during childbearing years. The reported incidence of VTE during pregnancy from developed countries ranges between 1 and 2 cases per 1000 pregnancies. The risk of deep venous thrombosis is five times higher compared to non-pregnant women. The predisposing factors for VTE in pregnant women are different from that in non-pregnant women. Furthermore, hospitalized women are a diverse group of patients with various risk factors for developing VTE.

Searching the literature, there is a paucity of reports from this part of the world. A retrospective study at King Abdul Aziz University Hospital determined the incidence and risk factors of VTE among hospitalized medical patients. The study showed that the most common risk factors were prolonged immobilization, surgery, post-delivery, heart failure and malignancy (23%, 16%, 9%, 7% and 4%, respectively).

In a retrospective study, Essam et al. evaluated the utilization of thromboprophylaxis among hospitalized patients in medical and surgical wards, but obstetrics and gynaecology patients were not included. In addition, Al Dorazi examined the effect of education on VTE prophylaxis practices.

The reported incidence of VTE in pregnancy and puerperium from KSA is 1.25 cases per 1000 deliveries. However, lack of post-mortem autopsy to confirm the diagnosis of suspected death related to VTE may contribute to under-estimation in our population. We were unable to locate any report in the literature addressing risk factors for VTE and the role of thromboprophylaxis in hospitalized women from the Arabian Peninsula.

Our institute is a referral hospital and has international accreditation; however, we do not have a VTE task force to standardize local policies and procedures for VTE risk assessment, implement clinical pathways for initiating thromboprophylaxis for at risk group or auditing the whole process. Furthermore, there is no risk assessment tool, whether on paper or electronically, to help physicians on busy days, and the decision to begin thromboprophylaxis is left to the discretion of the treating physician.

This study was designed to determine risk factors for developing VTE among hospitalized women in the Obstetrics and Gynaecology ward in Taibah University and to assess the treating physician’s adherence to thromboprophylaxis guidelines in the same group of patients by identifying the women at high risk for VTE according to expert haematologist and those who were offered thromboprophylaxis. By comparing this gap, we can encourage physicians to adapt risk assessment tools and to adhere to the available guidelines.

**Materials and Methods**

This is a retrospective study, conducted in the Haematology Department at King Abdulaziz University Hospital following approval of the hospital ethics committee. One hundred eighty-eight consecutive patients were included. Patients with a hospital length of stay greater than 1 day admitted to the Obstetrics and Gynaecology ward were included. The study group was recruited over a period of four months. Venous thromboembolism (VTE) risk stratification was evaluated. Patients eligible for thromboprophylaxis were compared to patients who received thromboprophylaxis.

**Exclusion criteria**

Patients admitted with a diagnosis of acute DVT and/or PE were excluded from the study as well as patients with a known thrombophilic condition.

**Setting and protocol**

Data collected from medical records include age, BMI, parity, recent surgery, immobility, varicose veins, active cancer, cardiac or respiratory diseases, acute infection, hormonal treatment, previous VTE or family history of VTE and prescribed pharmacological thromboprophylaxis.

Patients eligible for thromboprophylaxis were compared to patients given thromboprophylaxis.
The decision to start thromboprophylaxis was made by an independent expert haematologist. In gynaecological patients, the expert used the Caprin risk assessment model (RAM) to evaluate patients admitted for surgical reasons the Padua RAM to evaluate patients admitted for medical reasons, while the Royal College of Obstetrics and Gynaecology (RCOG) RAM was used to evaluate obstetric patients.13–17

Main outcome measure

Adherence to thromboprophylaxis guidelines based on agreement between patients eligible and patients who received thromboprophylaxis in the study group.

Statistical analysis

The analysis included all eligible patients. All statistical analyses were performed using SAS version 17.0, SPSS, Inc., Chicago, IL). Descriptive statistics are presented as the mean and percent, while correlation was tested using the Pearson correlation test where correlation is significant at the 0.01 level.

Results

A total of 188 patients were included in the study. The age of the participants ranged from 17 to 81 years. Sixty-one percent of the patients were admitted for gynaecological reasons, while 38% were admitted to the obstetrics ward (Table 1). The most common risk factors for developing VTE in gynaecology patients were surgery, obesity, malignancy and heart diseases (75%, 24%, 20% and 13%, respectively), while the most common risk factors for obstetrics patients included caesarean section (C/S), obesity, pre-eclampsia and multiple pregnancy (36%, 18%, 4.2% and 4.2%, respectively) (Table 2).

Seventy-five percent (n = 87) of participants admitted to the gynaecology ward had surgery, while 25% (n = 29) were admitted for medical reasons (Figure 1). Sixty-three percent (n = 46) of pregnant women delivered by spontaneous vaginal delivery, while 36% (n = 26) delivered by C/S and one patient had an abortion.

Forty-seven percent of all patients were eligible for thromboprophylaxis, while only 39% received thromboprophylaxis (Table 3). When patients were divided into obstetrics and gynaecology patients, 54% of gynaecological patients and 37% of obstetrics patients were eligible for thromboprophylaxis, while only 48% of gynaecological patients and 26% of obstetrics patients was prescribed thromboprophylaxis by their treating physician (Table 3).

Using the Pearson correlation test, adherence to thromboprophylaxis in all patients was 33%, 40% for gynaecological patients and only 14% for obstetrics patients (Table 3).

Discussion

Venus thromboembolism (VTE) is a common disease, and it is associated with potentially life-threatening complications and a high recurrence rate.12 The Incidence rates are higher in women during childbearing years compared to men of similar age.2 VTE is a multi-factorial disease, involving interaction between acquired and inherited risk factors.13 Pregnant women are 4–5 times more likely to develop VTE than non-pregnant women.3 Hospitalized women are a diverse group of patients, and the predisposing factors for VTE in pregnant women are different from those in non-pregnant women. The reported incidence of VTE from most developed countries ranges between 1 and 2 cases per 1000 pregnancies, which is similar to the range in KSA.12,15

All three components of Virchow’s triad, i.e., venous stasis, hypercoagulability and endothelial wall damage, occur during pregnancy.16 This hypercoagulable state is an adaptive mechanism to reduce the risk of haemorrhage during and after delivery. Risk factors for VTE can be divided into general risk factors, maternal risk factors and those specifically related to pregnancy.17 General risk factors include hospitalization for surgery or acute medical illness, active cancer, neurological disease, trauma or fracture.18 Maternal risk factors include age, obesity, parity, ethnicity, personal and family history of VTE and thrombophilia.19 The risk for VTE increases in women aged 35 years and older.20 Data from the UK Obstetric Surveillance system identified obesity and multiparity as

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**Table 1: Demographic data of all patients included in the study including patient’s type, age and body mass index (BMI).**

| Type of patients | N = 188 | Frequency | Mean | Std. deviation |
|------------------|---------|-----------|------|---------------|
| Obstetrics       | 72      | 38.3%     | Age 33.2 | 6.4 |
|                  |         |           | BMI 28.9 | 7.2 |
| Gynaecology      | 116     | 61.7%     | Age 45.5 | 6.4 |
|                  |         |           | BMI 28.1 | 6.8 |

**Table 2: Risk factors in our study compared to *Rehmani’s study**

| Risk factors | All patients | Gynaecology | Obstetrics | *Rehmani |
|--------------|--------------|-------------|------------|----------|
| N = 188      | N = 116      | N = 72      | N = 320    |
| Surgery      | 113 (60%)    | 87 (75%)    | 26 (36%)   | 36 (32%) |
| *BMI > 30    | 42 (22%)     | 28 (24%)    | 13 (18%)   | 134 (42%)|
| Malignancy   | 24 (20.7%)   | 24 (20.7%)  | NA         | 10 (3%)  |
| Heart disease| 18 (9.5%)    | 16 (13.8%)  | 2 (2.8%)   | 0        |
| Pre-eclampsia| 3 (4.2%)     | NA          | 3 (4.2%)   |          |
| Pregnancy    |              |             |            | 266 (83%)|
| Hyperemesis  | 2 (2.8%)     | NA          | 2 (2.8%)   |          |
| Multiple     | 3 (4.2%)     | NA          | 3 (4.2%)   |          |
| infections   |              |             |            |          |
| Heart disease| 4 (2%)       | 16 (13.8%)  | 2 (2.8%)   | 7 (2%)   |
| Lung disease | 1 (0.5%)     | 0           | 1 (1.4%)   | 0        |
| Renal        |              |             |            |          |
| PMH of VTE   | 2 (0.1%)     | 1 (0.9%)    | 1 (1.4%)   | 0        |
| OCCP *        | 1 (0.5%)     | 1 (0.9%)    | 0          | 3 (0.9%) |
| Immobility   | 0            | 0           | 1          | 0 (0.3%) |
major risk factors for pulmonary embolism. Pregnancy related factors include those from before conception such as hormonal stimulation, those during pregnancy such as hyper-emesis, twin pregnancy, pre-eclampsia and those related to mode of delivery. Caesarean section (C/S) is associated with increased immobility, prolonged hospital stays and obstetric complications. Elective caesarean section has been found to be associated with a doubled risk of VTE compared to vaginal delivery.

In non-pregnant women, the risk for developing VTE includes general risk factors as well as oral contraceptive pills or hormonal replacement therapy. VTE is the second most common cause of deaths in patients with active cancer. It is well established that women with gynaecological malignancies are at high-risk for developing VTE due to the malignancy itself, advanced age, pelvic mass, lengthy surgery, and thrombogenic chemotherapy. The reported rate of VTE in patients with gynaecologic malignancies ranges from 11% to 18%.

In KSA, pulmonary embolism is the second leading cause of maternal death. Rahmani et al. studied VTE risk factors and evaluated the adherence to VTE prophylaxis guidelines. The study included patients form surgical, medical and obstetrics and gynaecology wards. The most common risk factors were pregnancy, obesity and surgery (83%, 42% and 11%, respectively). In our study, the most common risk factors for developing VTE in all patients were surgery, obesity, and malignancy (60%, 22%, 20.7% respectively). Among gynaecological patients, surgery, obesity, malignancy and heart diseases (75%, 24%, 20% and 13.8%, respectively) were the common risk factors, while the most common risk factors for obstetrics patients included C/S, obesity, pre-eclampsia and multiple pregnancy (36%, 18%, 4.2% and 4.2%, respectively) (Table 2). The difference in risk factors for VTE might be because Rahmani et al. pooled obstetrics and gynaecology patients together. Caprini’s RAM was used for all patients and the decision to start thromboprophylaxis was made according to the American College of Chest Physicians (ACCP) guidelines.

Figure 1: Gynaecological patients classified according to received treatment modalities.

| Table 3: Patients eligible for thromboprophylaxis in obstetrics and gynaecology ward. |
|---------------------------------------------------------------|
|                                | All patients | Gynaecology | Obstetrics |
| Eligible for prophylaxis       | Number (%)   | Number (%)  | Number (%) |
|                                | 90 (47%)     | 63 (54%)    | 27 (37.5%) |
| Received prophylaxis           | 75 (39%)     | 56 (48%)    | 19 (26%)   |
| Pearson Correlation            | 0.33         | 0.40        | 0.14       |

The majority of organizations advise that pregnant women with more than one additional risk factor should be considered for thromboprophylaxis. Furthermore, The ACCP, the American Society of Clinical Oncology and the national guidelines recommend thromboprophylaxis for hospitalized patients with active cancer on chemotherapy and patients undergoing major surgery.

In the UK, following the publication of the first RCOG guidelines for VTE prophylaxis, a fall in maternal death secondary to VTE was observed. Despite the available guidelines for thromboprophylaxis, implementation of these guidelines is inconsistent. The Epidemiologic International Day for the Evaluation of Patients at risk for a Venus Thromboembolism in the Acute Hospital Care
Setting (ENDORSE) Study found that adherence to thromboprophylaxis was 58.5% among surgical patient and 39% among medical patients at risk. Limited data addressed adherence to thromboprophylaxis specific to pregnant and non-pregnant women. Rahmani evaluated the adherence to thromboprophylaxis guidelines in a Saudi population. Fifty-six percent of all patients were at risk for VTE but only 39.3% received prophylaxis. However, in the same study 83.1% of obstetrics and gynaecology patients were judged to be at risk for VTE, but only 53% received prophylaxis. In our study, adherence to prophylaxis in all patients was 33% which is less than the rate found by Rahmani, which could again be explained by the different RAM used. Furthermore, the RCOG guidelines for thromboprophylaxis were used in our study of pregnant women. When patients were divided into gynaecological and obstetrics patients, better adherence was seen among gynaecological patients than obstetrics patients. Gynaecology patients could have been better identified as high-risk patients as the majority of patients in this group were either surgical patients or oncology patients where RAM and thromboprophylaxis guidelines are well established. Furthermore, as this is a referral centre, gynaecology patients are usually complicated cases with comorbidities and obvious high risk for developing VTE.

Reasons for guideline under-utilization include underestimation of the VTE risk, failure to perform risk assessments and lack of awareness of relevant guidelines. An accurate estimation of the risk of thrombosis without the aid of risk assessment tools is not easy. Effective strategies for improving practice includes implementation of a multi-tiered strategy such as education, dissemination of guidelines, the use of risk assessment charts, automated reminders or clinical decision support system, and regular audit with feedback to the hospital staff.

The lack of a risk assessment tool upon hospital admission as part of organizational policy could explain the poor adherence to thromboprophylaxis in our institute. Furthermore, treating physicians’ concern about the bleeding risk associated with pharmacological thromboprophylaxis may be another cause of inappropriate practice. Moreover, underutilization of mechanical thromboprophylaxis occurs despite the ACCP recommendations.

In KSA, approximately 50% of obstetrics patient failed to receive thromboprophylaxis when it was indicated. Therefore, experts from around the country reviewed all published international guidelines and created an algorithm with the recommended prophylactic measures for any patient. Dissemination of this simplified RAM could help physician adherence to available guidelines.

Conclusions

Venous thromboembolism is associated with substantial morbidity and mortality and is largely preventable. Despite available RAM and guidelines, appropriate prophylaxis is vastly underutilized. To improve survival in pregnant and non-pregnant women, continuing medical education, dissemination of guidelines and regular clinical audits are necessary measures. Furthermore, implementation of a risk stratification tool is essential to identify at-risk women who would benefit from thromboprophylaxis, so the appropriate prophylaxis can be provided.

Study limitations

The type of study and the number of patients limits the study. Furthermore, our study is limited to a single centre, thus our experience may not be generalizable to other centres. Recommendation for follow up studies: Post-implementation outcome studies are recommended after the dissemination of the new national guidelines.

Conflict of interest

The author has no conflict of interest to declare.

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