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EPIDEMIOLOGICAL PROFILE OF THROMBOEMBOLIC DISEASE IN PREGNANT WOMEN IN OBSTETRIC INTENSIVE CARE UNIT

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Introduction :

Thromboembolic disease during pregnancy is a common condition responsible for significant morbidity and mortality. It is characterized by a complex pathophysiology and variable clinical presentation. The positive diagnosis is mainly based on paraclinical examinations and management is multidisciplinary.(1.2)

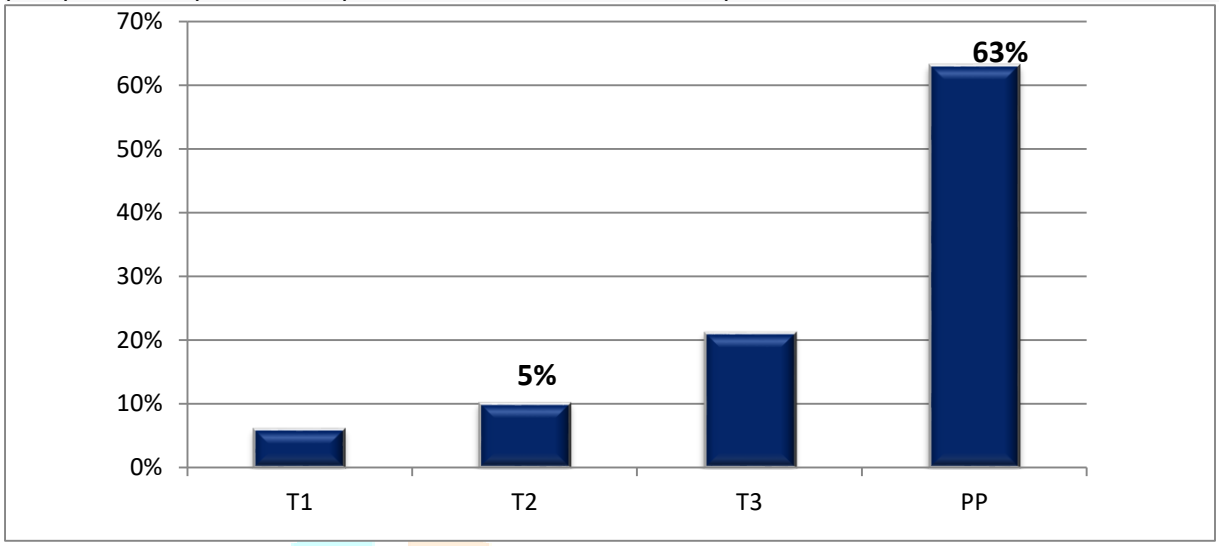
The objectives of our work were to study the epidemiological profile of thromboembolic disease during pregnancy and postpartum, as well as its clinical, paraclinical, and etiological characteristics; to determine the main risk factors; to propose a diagnostic approach and to establish a therapeutic scheme adapted to our context.

Material and methods:

Our study is a retrospective descriptive and analytical study of patients with venous thrombosis during the gravid-puerperal period, conducted at the Obstetric Intensive Care Unit of the Ibn Rochd University Hospital Center in Casablanca, over a period of 5 years, from January 1st, 2012 to December 31st, 2016, with a total of 49 patients. The inclusion criteria included all patients who had a confirmed thromboembolic event during pregnancy or postpartum with an exploitable medical record. The exclusion criteria were an unusable medical record, patients who had progressive thrombosis before pregnancy, and patients in whom the diagnosis was suspected but not confirmed by additional tests

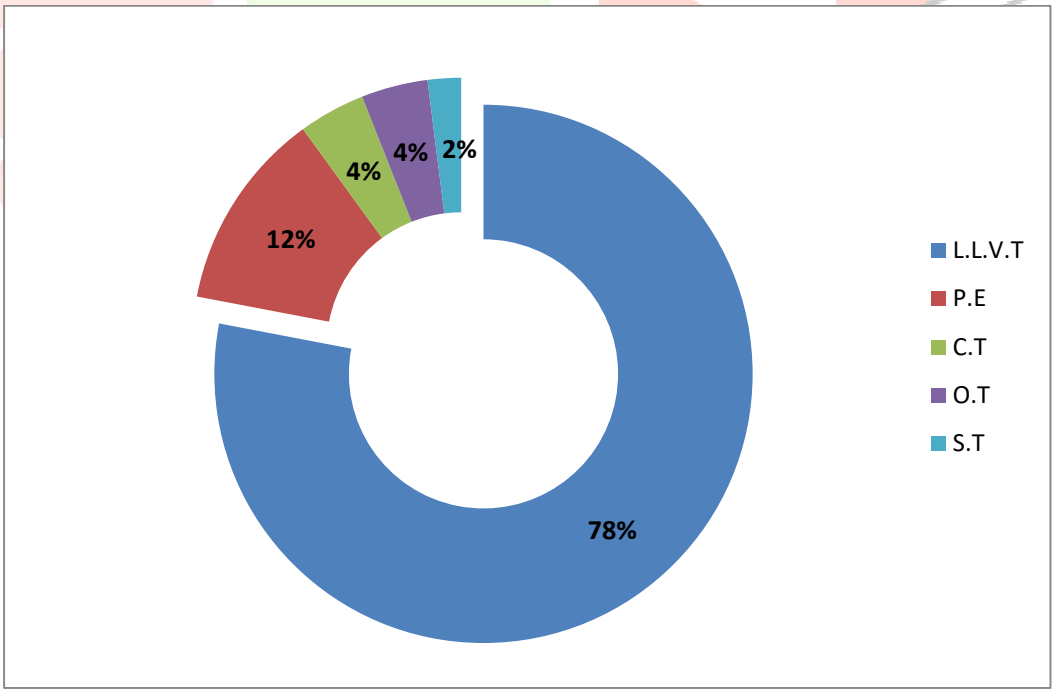
Results

The average age of our patients at the time of diagnosis was 29 years, ranging from 19 to 42 years old. Venous thromboembolic disease occurred during the antepartum period at varying frequencies, but the postpartum period represented the elective period with a rate of 63% of cases.



Graph 1 : Distribution of thromboembolic disease according to the time of onset

The clinical manifestations were dominated by venous thrombosis of the lower limbs, occurring in 38 patients (78%), followed by pulmonary embolism in 6 patients, cerebral thrombophlebitis in two patients, ovarian thrombosis in two patients, and one case of splenic vein thrombosis.



Graph 2 : Distribution of cases according to the location of the thrombosis.

Deep vein thrombosis (DVT) of the lower limbs occurred on the left side in 62% of cases. The diagnosis was suspected clinically based on an increase in limb volume, redness, pain, a decrease in ballottement, and a positive Homans sign. It was confirmed by lower limb venous Doppler ultrasound, which showed thrombosis in all patients, with extension of the thrombus from the popliteal vein to the external iliac vein.

As for pulmonary embolism (PE), it occurred in six patients. All cases were noted in the postpartum period, with a delay of 15 days after delivery. Clinical indications included dyspnea, chest pain, and tachycardia. The diagnosis was confirmed by thoracic angioscanner, which showed dilation of the pulmonary artery or one of its branches

Cerebral thrombophlebitis was noted in two patients, revealed in the first patient by a generalized tonic-clonic seizure with post-critical coma, and in the second patient by a decrease in visual acuity and headaches. The diagnosis was confirmed by magnetic resonance imaging of the brain.

Two cases of ovarian vein thrombosis were reported. The first occurred in the second trimester and was revealed by pain in the right iliac fossa, accompanied by fever and abdominal guarding on clinical examination. The diagnosis was confirmed by abdominal angioscanner. The second case occurred in the postpartum period, one week after a vaginal delivery at home that was complicated by postpartum hemorrhage due to cervical injury. The patient also presented with pain in the right iliac fossa, fever, and abdominal guarding on clinical examination, with a suspected appendiceal abscess on ultrasound. A laparotomy was performed, revealing a dilated ovarian vein.

The course was marked by the appearance of significant abdominal distension accompanied by vomiting and diarrhea on postoperative day 2, followed by the patient's death on day 6 in a septic shock state. Only one case of splenic vein thrombosis was reported. It occurred during the second trimester and was revealed by acute respiratory distress with abdominal guarding on physical examination. The diagnosis was confirmed by abdominal angioscanner, which revealed dilation of the portal system and splenic vein with partial mural thrombus of the superior lobular splenic vein.

The reason for consultation depended on the location of the thrombosis: 38 patients had presented with swelling of the lower limbs, 6 with chest pain and dyspnea, 3 with abdominal guarding on physical examination. One patient had presented with a seizure with impaired consciousness, and the last patient had a presentation of decreased visual acuity with headaches.

The main complementary exams performed were lower limb venous Doppler ultrasound, thoracic and abdominal angioscanner, and cerebral MRI.

As for the etiological diagnosis, classical risk factors were dominated by bed rest, history of thromboembolic disease, and varicose veins. As for obstetrical risk factors, they were dominated by multiparity, hormonal contraception, and preeclampsia.
Thrombophilia screening, both constitutional and acquired, was only requested in 12 patients before starting anticoagulant therapy. It was negative in eight patients, while four abnormalities were identified, including protein C and S deficiency, isolated protein S deficiency, antithrombin III deficiency, and the presence of antiphospholipid antibodies.

On the therapeutic side, elastic compression stockings were prescribed for all patients, in addition to anticoagulant therapy based mainly on heparins and vitamin K antagonists. During the first trimester, patients were treated with heparin. During the second and third trimesters, the parturients were treated with low-molecular-weight heparin or unfractionated heparin, with a switch to vitamin K antagonists within the first 24 hours. The latter were stopped at 35 weeks of gestation and resumed 24 hours after delivery
The evolution under anticoagulant treatment was generally favorable in 94% of cases. However, three patients died: one as a result of cerebral thrombophlebitis, another due to splenic thrombosis, and the third due to ovarian vein thrombosis. Additionally, disappearance of clinical signs was observed between the 4th and 6th day of treatment. Ultrasound Doppler control performed between day 10 and 15 of treatment showed recanalization or a beginning of recanalization of the venous network in all cases. However, some complications occurred, including septic shock in one case, three cases of pneumonia, one case of blindness, and one case of bedsores

DISCUSSION

The incidence of venous thromboembolic disease during pregnancy has been widely discussed in several studies, but the risk of occurrence varies on average between 0.5 and 2.2 per 1000 pregnancies. In our series, the frequency of occurrence was 2 to 3 per 1000 pregnancies (3).

Author	Year	Country	Frequency
Jacobsen A. et al [8]	2008	NORWAY	1/1000 grossesse
James A. et al [7]	2006	USA	1,72/1000 grossesse
Helt J. et al [6]	2005	MINESOTA USA	1-2/1000 grossesse
Mc Coll. et al [17]	1979	UK	0,71/1000 grossesse
Méta-analyse [22]	2015	USA	1,2/1000 grossesse
Kane. et al [23]	2013	ESCOTLAND	1,3/1000 grossesse
Notre étude	2015	MOROCCO	2-3/ 1000 grossesse

Table 1 : The frequency of thromboembolic disease during pregnancy in several studies

This risk increases gradually during pregnancy and up to six weeks postpartum, but the risk is higher during the third trimester and the first three weeks postpartum, which is consistent with our study(4)

Frequency	Chan. et al[24]	Ray J. et al [19]	David J. et al [25]	Our study
Antenatal	51%	66%	48,80%	37%
Postpartum	49%	34%	51,60%	63%

Table2 : comparing the frequency of venous thrombosis according to the period of occurrence during pregnancy

The age group most responsible for thrombosis is that of women over 35 years old. This is likely due to the increased prevalence of other added risk factors, including cesarean deliveries, hypertension, heart disease, and obesity. (In our study, venous thromboembolism occurred in 21% of patients over 35 years old.(5)

	Jang MJ [34]	David J [25]	Jacobsen [8]	Our study
<24year	4%	26%	16%	30%
25-30 year	32,6%	26%	33%	32%
30-35year	39,4%	24%	32%	17%
>35year	24%	24%	19%	21%

Table 3: comparing the frequency of venous thromboembolism according to the age of the parturient

The main classical risk factors are dominated in the literature by personal history of venous thrombosis, age over 35, prolonged bed rest, and obesity, which is consistent with our results

Pre-existing risk factors	OR (IC95%)
Personal history of venous thrombosis	24,8 (17-36)
Obesity	
Antepartum thrombosis	1,8 (1,3-2,4)
Postpartum thrombosis	2,4 (1,7-3,3)
Age >35 year	2,1 (2,0-2,3)
Smoking	
Antepartum thrombosis	2,1 (1,3-3,4)
Postpartum thrombosis	3,4 (2,0-5,5)
Diabetes.	2,0 (1,4-2,3)
Higher blood pressure	1,8 (1,4-2,3)

Table 4 : Classical risk factors for pregnancy-related venous thromboembolism

As for obstetric risk factors, they are mainly dominated by pre-eclampsia, the occurrence of postpartum hemorrhage or infection, as well as multiparity, emergency cesarean section, and assisted reproductive technology

Risk factors associated with pregnancy	**OR (IC95%)**
Twin pregnancy	2,6 (1,1-6,2)
Immobilization	
Antepartum thrombosis	7,7 (3,2-19)
Postpartum thrombosis	10,8(4,0-28,8)
assisted reproductive technology	
Singleton pregnancy	4,3 (2,0-9,4)
Twin pregnancy	6,6 (2,1-21,0)
C-section	
schedueld	1,3 (0,7-2,2)
emergency	2,7 (1,8-4,1)
postpartum hemorrhage	
Without surgery	4,1 (2,3-7,3)
With surgery	12 (3,9-36,9)
Infection	
Normal delivery	20,2 (6,4-63,5)
C-section	6,2 (2,4-16,2)
Pre-eclampsia	
Without intrauterine growth retardation.	3,1 (1,8-5,3)
With intrauterine growth retardation.	5,8 (2,1-16,0)

Table 5 : risk factors associated with pregnancy for venous thromboembolism

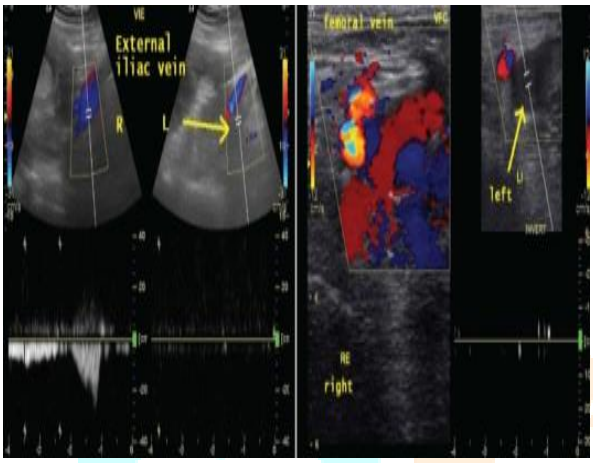
The main abnormalities found in thrombophilia testing are represented by antithrombin III deficiency, mutation of the prothrombin gene, and resistance to activated protein C or factor V(6). This does not match our results, but our sample size was not significant since we only requested the test for 12 patients.

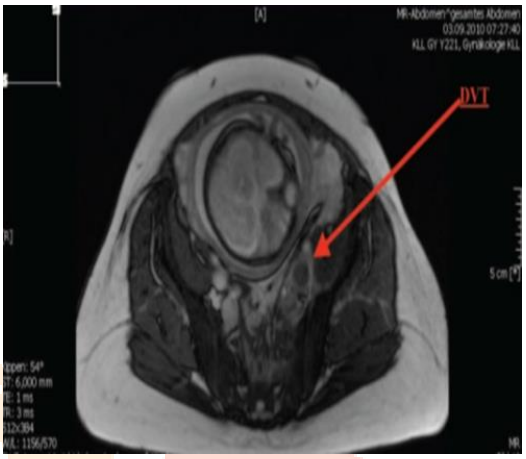
	Tison [53]	**Roldan [54]**	**Minetti [50]**	**Our Study**
Protein C Deficiency	4 à 14%	3%	1,70%	2%
Protein S Deficiency	1,30%	3%	7%	4%
Antithrombin Deficiency	2 à 6%	-	3%	2%

Table 6 : comparing constitutional deficits found in our study with the literature

Deep vein thrombosis of the lower limbs CLINICALLY: □ Increased volume of the lower limbs □ Pain on palpation of the venous path □ Decreased bouncing □ Positive Homans sign PARACLINICALLY: □ D-Dimers: non-specific □ Doppler ultrasound of the lower limbs □ Phlebography and Magnetic resonance imaging

The positive diagnosis is made by venous Doppler ultrasound of the lower limbs, which looks for an image of thrombus, as well as indirect signs such as incompressibility of the vein, immobility of the wall, and venous dilation. The Doppler also looks for a slowing or absence of blood flow indicating partial or complete obstruction. However, the Doppler remains limited for ilio-caval thromboses, hence the importance of resorting to phlebography and magnetic resonance imaging.

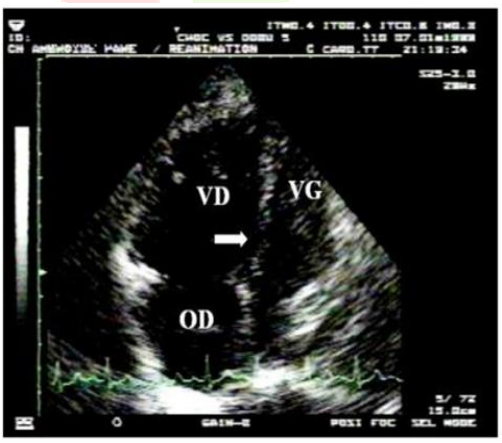


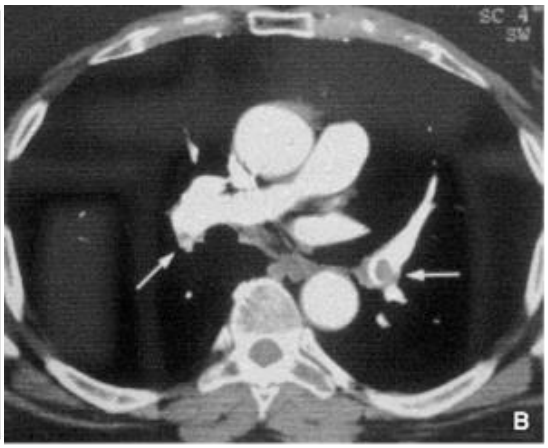


Picture 1 : Venous Doppler ultrasound **Picture 2: Venography**

D-dimers are not specific during pregnancy as they are physiologically elevated.

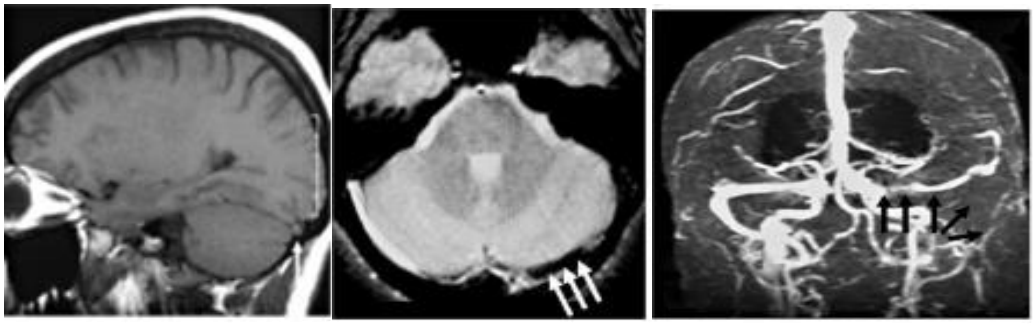
Pulmonary embolism, the second most common location during pregnancy after lower limb DVT, has a polymorphic clinical presentation, ranging from simple tachycardia, cough, or chest pain often considered benign, to respiratory distress with signs of right heart failure. Its diagnosis is mainly based on thoracic angioscanner, which is the examination of choice but is not used as first-line due to its fetal and maternal irradiation(7,8,9) It allows the diagnosis by locating the thrombus and determining its extension, but also identifying an alternative diagnosis if pulmonary embolism is excluded. Other tests may be prescribed, including lower limb doppler ultrasound, cardiac ultrasound, chest X-ray, and ECG.





Picture 3: Trans-thoracic echocardiography **Picture 4: Thoracic CT angiography**

Concerning cerebral thrombophlebitis, the clinical symptoms are varied but are dominated by headaches of variable intensity, alone or associated with neurological deficits, epileptic seizures, alterations in consciousness or increased intracranial pressure(10,11,12). The positive diagnosis is based on venography or magnetic resonance imaging in T2 sequence, showing an image of thrombosis in the venous sinuses or cortical veins(13).



a: Para-sagittal slice of MRI sequence T1 showing an iso-signal; b: Typical appearance of cerebral venous thrombosis; c: Frontal slice of a venography showing occlusion of the sinus.

Ovarian thrombosis is rare, and can manifest as lower back or pelvic pain, or respiratory distress. The diagnosis is made by abdominal angioscanner. Other locations may also be found, such as splenic or portal thrombosis(14).

Therapeutic management of venous thrombosis depends on the timing of onset and patient's condition, and primarily involves mechanical means such as elastic compression stockings, and medical measures dominated by heparins and vitamin K antagonists. Thrombolysis and surgery are rarely indicated and reserved for situations of proximal deep vein thrombosis and massive pulmonary embolism that threaten life. However, in general, during the first trimester, all patients are put on heparin due to contraindications to vitamin K antagonists(15).

During the second and third trimesters, low molecular weight heparin or unfractionated heparin is used, with a switch to vitamin K antagonists within the first 24 hours. The latter are stopped around the 34th or 35th week and restarted immediately postpartum if conditions permit.

Several scores have been established for the prevention of venous thromboembolism, the most recent being the American College of Chest Physicians in 2012, which defined global risk as very high, high, moderate, or undefined based on clinical and biological risk factors.

Prevention during pregnancy and postpartum is only recommended in cases of very high or high risk, while in cases of moderate risk it is only indicated postpartum. For undefined risk, the decision is made on a case-by-case basis and is based either on treatment with low molecular weight heparin or on simple surveillance(15).

The course of deep vein thrombosis is generally favorable if early intervention is taken, although complications may occur, including progression to pulmonary embolism or short-term death, post-thrombotic syndrome, and long-term recurrence(16).

Conclusion:

Venous thromboembolic disease represents one of the main complications of the gravid-puerperal period. A good understanding of its pathophysiology allows for better clinical, paraclinical, and therapeutic approaches. The search for classic and obstetric risk factors, as well as thrombophilia screening, remains the cornerstone of secondary prevention. Better awareness of pregnant women can reduce the incidence of this pathology.

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