West Middlesex University Hospital

Date of Search: 29 Aug 2017
Sources Searched: Medline, Embase, Oxford Medicine Online, DynaMed Plus.

Venous Thromboembolism (VTE) and First Trimester Pregnancy/Abortion

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Evidence Summary:

- Pregnancy represents a hypercoagulable state beginning as early as the first trimester and is a risk factor for venous thromboembolic events.
- Risk of venous thromboembolism may be highest in third trimester and postpartum period, especially in first week postpartum.
- A retrospective crossover-cohort study published in the NEJM study (2014) reported significant increases in risks for primary thrombotic events beyond the 6-week postpartum period in high risk women. However, the absolute increases in risk from 7 to 12 weeks after delivery were small.
- It is unclear as to whether women undergoing surgical management of miscarriage or termination of pregnancy are at increased risk of VTE. As such, there is currently no consensus regarding the use of thromboprophylaxis for these patients.
- Transient increases in fibrinolytic and thrombotic activity in the immediate period following first trimester induced abortion have been demonstrated.

Sources: DynaMed Plus [Internet]. Ipswich (MA): EBSCO Information Services. 1995 - . Record No. 901146, Venous thromboembolism (VTE) in pregnancy; [updated 2014 Jul 01, cited **30/08/2017**]; [about 15 screens]. Available from http://www.dynamed.com/login.aspx?direct=true&site=DynaMed&id=901146 . Registration and login required.]

1. Fibrin(ogen) degradation products and thrombin-antithrombin complex before and after voluntary pregnancy interruption

Author(s): Manoni F.; Gessoni G.; Antico F.; Antico A.; Valverde S.; Rossito G.; Sartori R.

Source: European Journal of Laboratory Medicine; 1994; vol. 2 (no. 3); p. 179-183

Publication Date: 1994

Publication Type(s): Article

Abstract: Background. Pregnancy is characterized, in the third trimester, by a hypercoagulative state. The hemostatic balance, modified in a thrombophilic way, is considered physiological, since it prevents damage to the maternal and fetal circulation. We studied plasma levels of direct markers of fibrinolysis, such as fibrin degradation products (FbDP) and fibrinogen degradation products (FgDP), and an indirect marker of thrombin production and inactivation, the thrombin-antithrombin III complex (TAT), before and after voluntary pregnancy interruption (VPI) during the first trimester of pregnancy. Methods. Modifications in the hemostatic-fibrinolytic balance after VPI were evaluated by determining plasma FgDP and FbDP, total degradation products (TDP) and TAT by ELA. We studied 55 healthy women who were not pregnant (control group) and 87 pregnant women within the tenth week of gestation (in 45 patients blood samples were taken basally and 3 hours after VPI; in 42 basally and 24 hours after VPI). Results. We found no significant difference between the levels of pregnant women before VPI and those of the control group. A comparison between basal data and those obtained 3 hours after VPI showed a significant increase in all parameters. In the group of 42 patients, 24 hours after VPI, concentrations of FgDP, FbDP and TDP decrease compared to the group of 45 patients 3 hours after VPI, remaining higher than basal levels in same subjects. Conclusions. The evolution of FbDP, FgDP, TDP and TAT show that in the first ten weeks of pregnancy, plasmin activity and TAT are not significantly different from those in controls. Three hours after VPI, fibrinolytic markers prevail with respect to the fibrinogenolytic ones. TAT increases 3 hours after VPI, returning to normal 24 hours after.

Database: EMBASE

2. Increase of plasma tissue-plasminogen activator antigen levels after induced abortion

Author(s): Yoshimura T.; Nakamura T.; Ito M.; Kawasaki N.; Okamura H.

Source: La Ricerca in clinica e in laboratorio; 1991; vol. 21 (no. 1); p. 91-93

Publication Date: 1991

Publication Type(s): Article

PubMedID: 1907762

Abstract: We previously reported that plasma thrombotic activity is transiently increased immediately after induced abortion. However, changes in the fibrinolytic system have not yet been studied. Plasma tissue-plasminogen activator (t-PA) antigen levels were studied before and after abortion induced during the first trimester of pregnancy. Compared with the preoperative level (1.68 +/- 0.15 ng/ml), t-PA level was significantly increased (2.78 +/- 0.55 ng/ml, p less than 0.01) 15 min after the induced abortion, while it almost returned to the preoperative values (2.09 +/- 0.40 ng/ml) 2h later. This finding suggests that fibrinolytic activity is transiently increased immediately after the induced abortion, acting as a defense mechanism against thrombosis. Tissue-plasminogen activator (tPA), a protease enzyme that activates the thrombolytic system, and that is known to rise after term delivery, was assayed in 9 women undergoing therapeutic abortion by dilation and curettage. The assay was an ELISA (enzyme-linked immuno-sorbent assay) kit from Biopool AB, Umea, Sweden. The women had received atropine and iv thiamylal anesthesia. The blood was collected in citrate with a 21 gauge needle before, 15 min and 2 hours after surgery, frozen, and assayed simultaneously. t-PA levels were 1.68 ng/mi before, 2.78 ng/mi in 15 minutes (p0.01), and

2.09 ng/mi 2 hours after curettage (n.s.). These results reflect the previously reported increase in fibrin peptide A levels, indicative of thrombin activity, just after abortion.

Database: EMBASE

3. Modifications induced on thrombin and plasmin activity by voluntary interruption of pregnancy.

Author(s): Manoni, F; Gessoni, G; Antico, A; Finesso, P; Rossito, G; Sartori, R

Source: Minerva ginecologica; May 1993; vol. 45 (no. 5); p. 245-250

Publication Date: May 1993

Publication Type(s): English Abstract Journal Article

PubMedID: 8351063

Abstract: Pregnancy is characterized by plasmatic variations of coagulative factors' concentration and by different haemostatic-fibrinolytic balance. At present it is possible, with EIA methods, to measure fibrinogen (FgDP) and fibrin (FbDP) degradation products with precision and accuracy, as direct indexes of fibrinolysis and the thrombin-antithrombin III complex (TAT) as indirect index of thrombophilia. We have considered the course of those indexes in 61 pregnant women within the tenth week of gestation, before and after voluntary pregnancy interruption (VPI) resulted without complications. The results don't show any peculiar variation of the examined parameters between the pregnant women before VPI and a control group. Comparing the basal data with those obtained three hours after VPI, all indexes are increased, particularly FbDP. After 24 hours the concentration of FgDP, FbDP and TDP decreased in comparison with the three hours control drawing, nevertheless staying higher than the values obtained in the basal drawing. The evolution of FDP and of TAT, in our study, points out that, in the first weeks of pregnancy, the haemostatic-fibrinolytic balance does not differ significantly from the physiological balance. Three hours after VPI fibrinolytic mechanisms prevail as regards the fibrinogenolytic ones. TAT increases after 3 hours and returns to the rules after 24 hours, proposing itself as an indirect index of thrombinic activation and as a direct index of antithrombinic activity.

Database: Medline

4. Sudden increase of plasma fibrinopeptide A levels after induced abortion.

Author(s): Yoshimura, T; Ito, M; Kawasaki, N; Matsui, K; Okamura, H

Source: La Ricerca in clinica e in laboratorio; 1987; vol. 17 (no. 3); p. 265-268

Publication Date: 1987

Publication Type(s): Journal Article

PubMedID: 3671998

Abstract: Plasma fibrinopeptide A levels were studied before and after abortion induced during the first trimester of pregnancy. Fibrinopeptide A levels were significantly increased 15 min after the induced abortion, and returned to preoperative values 2h later. This finding suggests that thrombotic activity is transiently increased immediately after the induced abortion. Activation of the clotting factors during the induced abortion appears to be important in controlling uterine hemorrhage. A recently developed assay of blood fibrinopeptide A was used to evaluate the coagulation system at the time of induced abortion in 10 women whose pregnancies were terminated at 5-11 weeks' gestation. Since fibrinopeptide A is the 1st substance split off from fibrinogen during thrombin-catalyzed fibrin formation, the presence of free fibrinopeptide A in the blood is a good indicator of thrombin activity. Before the induced abortion, the plasma fibrinopeptide A level of the 10 subjects was 6.4 + or - 4.3 ng/ml. A significant increase of this level (to 79.3 + or - 96.9 ng/ml) was observed in all patients 15 minutes after the abortion procedure. In 8

of the 10 patients, the level had dropped to 13.6 + or - 9.2 ng/ml 2 hours after the abortion. These findings suggest that an activation of the coagulation system occurs during induced abortion and may be important in controlling uterine hemorrhage. This process appears to be initiated by the release of tissue thromboplastin from the placenta or amniotic fluid into the maternal circulation. However, the blood clotting that accompanies induced abortion is considered to be a local phenomenon and the activated clotting factors are cleared immediately from the circulation without excess thrombus formation.

Database: Medline

5. Normal pregnancy is associated with an increase in thrombin generation from the very early stages of the first trimester.

Author(s): Bagot, C N; Leishman, E; Onyiaodike, C C; Jordan, F; Freeman, D J

Source: Thrombosis research; Jun 2017; vol. 157 ; p. 49-54

Publication Date: Jun 2017

Publication Type(s): Journal Article

PubMedID: 28692840

Abstract:BACKGROUND Pregnancy is a hypercoagulable state associated with an increased risk of venous thrombosis, which begins during the first trimester, but the exact time of onset is unknown. Thrombin generation, a laboratory marker of thrombosis risk, increases during normal pregnancy but it is unclear exactly how early this increase occurs.METHODSWe assessed thrombin generation by Calibrated Automated Thrombography in women undergoing natural cycle in vitro fertilization, who subsequently gave birth at term following a normal pregnancy (n=22). Blood samples were taken just prior to conception and repeated five times during very early pregnancy, up to Day 59 estimated gestation.RESULTS Mean Endogenous Thrombin Potential (ETP), peak thrombin generation and Velocity Index (VI) increased significantly from pre-pregnancy to Day 43 gestation (p=0.024-0.0004). This change persisted to Day 59 gestation. The mean of the percentage change from baseline, accounting for inter-individual variation, in ETP, peak thrombin and VI increased significantly from pre-pregnancy to Day 32 gestation (p=0.0351-<0.0001) with the mean increase from baseline persisting to Day 59 gestation.CONCLUSION Thrombin generation increases significantly during the very early stages of normal pregnancy when compared to the pre-pregnancy state. The increased risk of venous thrombosis therefore likely begins very early in a woman's pregnancy, suggesting that women considered clinically to be at high thrombotic risk should start thromboprophylaxis as early as possible after a positive pregnancy test.

Database: Medline

6. Changes in platelet aggregation during pregnancy and the immediate postpartum period

Author(s): Hussein B.; Maarouf A.; Gomez K.; Davies J.; Obeng-Tuudah D.; Riddell A.; Kadir R.

Source: Haematologica; Jun 2016; vol. 101 ; p. 827-828

Publication Date: Jun 2016

Publication Type(s): Conference Abstract

Available in full text at Haematologica - from National Library of Medicine

Abstract: Background: Platelet dysfunction is implicated in uteroplacental disorders. During the early stages of gestation platelets have important roles in the process of placentation. Platelet function contributes to enhanced haemostasis at delivery. However, there is limited data on the changes of platelet function during normal pregnancy. Understanding physiological changes of platelet aggregation during different stages of pregnancy is helpful for better understanding of pathophysiology of abnormal placentation. Aims: To assess platelet aggregation during three trimesters of pregnancy and immediate postnatal period in normal healthy women compared to control nonpregnant group. Methods: Cross-sectional cohort study including a total of 46 women: 10 participants for each trimester, 10 postnatal cases and 6 control non-pregnant women. Case selection was based on specific inclusion criteria. 30mL of venous blood was obtained from each participant following consent. Light transmission aggregometry was performed with Dual channel Payton 600B aggregometer using six platelet aggregating agonist (epinephrine, adenosine triphosphate, collagen, ristocetin, arachidonic acid and U46619). Results: The findings included reduced secondary aggregation curve appearance in pregnant and postnatal women when compared to control group, which was most apparent in the third trimester. Compared to non-pregnant controls, platelet aggregation induced by ADP and collagen were reduced during third trimester while epinephrine induced aggregation was reduced during the first trimester. Summary/Conclusions: Reduced platelet reactivity in response to epinephrine during early pregnancy can be considered as a mechanism to reduce thrombosis and allow normal placentation while diminished ADP and collagen induced aggregation in third trimester could be a compensatory mechanism since pregnancy associated with hyper-coagulation particularly in late stages.

Database: EMBASE

7. Normal pregnancy and coagulation profile: from the first through the third trimester.

Author(s): Ibeh, Nancy; Okocha, Chide Emmanuel; Aneke, Chinawaeze John; Onah, Christian Ejike; Nwosu, Agatha Oluchi; Nkwazema, Kenneth Amobi

Source: Nigerian journal of medicine : journal of the National Association of Resident Doctors of Nigeria; 2015; vol. 24 (no. 1); p. 54-57

Publication Date: 2015

Publication Type(s): Journal Article

PubMedID: 25807675

Abstract:BACKGROUND Normal pregnancy is a hypercoagulable state; a physiological safety valve aimed at preventing excessive maternal blood loss at delivery.OBJECTIVETo evaluate the influence of normal pregnancy on blood coagulation and to explore changes in activity from the first through the third trimester.SUBJECT AND METHODSSixty (60) apparently healthy pregnant women (20 from each trimester) and 20 healthy non-pregnant age-matched controls were recruited. Each participant had Prothrombin time (PT). Activated partial thromboplastin time (APTT) and platelet count done. Multiple comparisons were made between control values and coagulation profile at different stages of pregnancy using the Bonferroni statistics. Results were expressed as means and standard deviations, $p < 0.01$ was significant at 95 % CI. Ethical approval for the study was obtained from the Institutional review board.RESULTSThe means of the APTT were significantly lower in the first,

second and third trimesters compared with controls (35.59 ± 4.95 seconds, 32.22 ± 5.79 seconds and 29.60 ± 3.66 seconds, respectively, vs. 40.55 ± 5.95 seconds; p = 0.01). Correspondingly, the platelet count was significantly lower in the 3 trimester of pregnancy compared with controls (178.35 ± 41.52 x 10(9)/L vs. 233.86 ± 55.34 x 10(9)/L; p < 0.01) and equally with level in the 2nd trimester (178.35 ± 41.52 x 10(9)/L vs. 232.10 ± 48.67 x 10(9)/L; p < 0.01).CONCLUSIONThe APTT and platelet counts are significantly lower in the 3 trimester of normal pregnancy.

Database: Medline

8. Origin and levels of circulating microparticles in normal pregnancy: A longitudinal observation in healthy women.

Author(s): Radu, Claudia M; Campello, Elena; Spiezia, Luca; Dhima, Sonila; Visentin, Silvia; Gavasso, Sabrina; Woodhams, Barry; Cosmi, Erich; Simioni, Paolo

Source: Scandinavian journal of clinical and laboratory investigation; Oct 2015; vol. 75 (no. 6); p. 487-495

Publication Date: Oct 2015

Publication Type(s): Journal Article Observational Study

PubMedID: 26067611

Abstract:OBJECTIVEMicroparticles (MP) are actively involved in the hypercoagulable state reported both in normal pregnancies and in pregnancy diagnosed with placenta-mediated complications. In this study the origin and the levels of plasma MP as well as MP activity were evaluated in a group of healthy women during the three trimesters of a normal pregnancy.MATERIALS AND METHODSSeventy-five healthy normotensive pregnant women were enrolled and blood samples were prospectively collected at three different time points corresponding to 1st trimester, 2nd trimester, 3rd trimester of pregnancy. A group of age- matched healthy non-pregnant women acted as controls. Both standard clotting parameters and MP of different origin were measured. MP were identified by size and annexin V- FITC labelling using flow-cytometer. MP subtypes were identified using specific monoclonal antibodies. Procoagulant activity of MP was assessed using the STA® Procoag PPL assay.RESULTSThe levels of total, platelet-, endothelial-, leukocyte-derived and tissue factor-bearing MP, as well as the MP procoagulant activity, in non-complicated pregnancy were higher in the 1st trimester as compared to non-pregnant age-matched women. Regardless of the origin, MP levels gradually increase during pregnancy, with the highest values reached in the 3rd trimester.CONCLUSIONSMP levels gradually increase during normotensive pregnancy. All types of MP including TF+ present with the highest levels in the 3rd trimester. MP convey prothrombotic and proinflammatory antigens already from the first trimester of normal pregnancy. This may contribute to the global hypercoagulable state observed, particularly in the last months of pregnancy, also in healthy women.

Database: Medline

9. Combined hormonal contraception and risk of venous thromboembolism within the first year following pregnancy

Author(s): Petersen J.F.; Bergholt T.; Nielsen A.K.; Lokkegaard E.C.L.; Paidas M.J.

Source: Thrombosis and Haemostasis; 2014; vol. 112 (no. 1); p. 73-78

Publication Date: 2014

Publication Type(s): Article

PubMedID: 24499991

Abstract: Estimating the risk of venous thromboembolism (VTE) associated with combined hormonal contraceptives following early terminated pregnancies or birth, a Danish nationwide retrospective cohort observing a one-year follow-up was defined using three unique registries. All Danish women with confirmed pregnancies aged 15-49 during the period of 1995-2009 were included. The main outcomes were relative and absolute risks of first time venous thromboembolism in users as well as non-users of combined hormonal contraceptives. In 985,569 person- years, 598 venous thromboembolisms were recorded. After early terminated pregnancies and births, respectively, 113 and 485 events occurred in 212,552 and 773,017 person-years. After early terminated pregnancies, the crude VTE incidence ratios were similar, and the numbers needed to harm were equal between groups that did or did not use combined hormonal contraceptives throughout the follow-up year. After childbirth, individuals that used combined hormonal contraceptives were more likely than non-users to experience VTE depicted by crude incidence ratios; however, the difference was only significant after 14 weeks. This implied that the numbers needed to harm were lower for those that used compared to those that did not use combined oral contraceptives in the initial 14 weeks postpartum. In conclusion, the use of combined hormonal contraceptives after early terminated pregnancies was not detrimental, but during the puerperal period, they should be used with caution. © Schattauer 2014.

Database: EMBASE

10. What is the coagulation state during pregnancy?

Author(s): Zaporozhan V.; Tarabrin O.; Gavrychenko D.; Mazurenko G.; Shcherbakov S.

Source: European Journal of Anaesthesiology; Jun 2014; vol. 31 ; p. 105

Publication Date: Jun 2014

Publication Type(s): Conference Abstract

Available in full text at European Journal of Anaesthesiology - from Ovid

Abstract: Background and Goal of Study: Normal pregnancy is accompanied by changes in the coagulation and fibrinolytic systems. These changes may be important for reducing intrapartum blood loss, but they determine an increased risk of thromboembolism during pregnancy and puerperium. Materials and methods: We studied the coagulation system of 63 women with normal pregnancies. To compare the results were also studied the coagulation system of 67 healthy volunteers. This study was approved by the Research Ethical Board (3723-G) of Odessa National Medical University on 20 of May 2013. Monitoring of hemostasis was by low-frequency piezoelectric hemoviscoelastography (LPH). We measured the difference in the basic parameters of hemostasis, to ascertain the significant changes in the state of blood coagulation. Results and discussion: Aggregation index the intensity of the contact phase of coagulation was increased on 54.7% (p <0,05), the time the contact phase of coagulation on 39,8% (p <0.05) and initial rate of blood aggregation on 41,6% (p <0.05) which create a state hyperaggregation. Coagulation indexes: a constant thrombin activity was increased on 34.5% (p <0.05), the intensity of clot polymerization on 37,8% (p <0.05), the formation of platelet-fibrin clot structure on 41,6% (p <0.05), the intensity of

coagulation drive was increased on 29.2% (p <0.05) and maximum density of the clot was increased on 48.5% (p <0.05). All this results create a state of hypercoagulability. Also an fibrinolysis indicator the intensity of the retraction and clot lysis decreased by 44.7% (p <0.05), create a hypofibrinolytic state. Conclusion(s): Using our method, we confirmed the diagnosis of changes in the hemostatic system from initial viscosity and platelet aggregation to coagulation and lysis of clot. During normal pregnancy the hemostatic balance changes in the direction of hyperaggregation, hypercoagulability and hypofibrinolytic state.

Database: EMBASE

11. Risk of a thrombotic event after the 6-week postpartum period.

Author(s): Kamel, Hooman; Navi, Babak B; Sriram, Nandita; Hovsepian, Dominic A; Devereux, Richard B; Elkind, Mitchell S V

Source: The New England journal of medicine; Apr 2014; vol. 370 (no. 14); p. 1307-1315

Publication Date: Apr 2014

Publication Type(s): Research Support, N.i.h., Extramural Journal Article

PubMedID: 24524551

Available in full text at New England Journal of Medicine - from Massachusetts Medical Society ; Notes: Please select 'Login via Athens or your institution' and enter your OpenAthens username and password.

Abstract:BACKGROUNDThe postpartum state is associated with a substantially increased risk of thrombosis. It is uncertain to what extent this heightened risk persists beyond the conventionally defined 6-week postpartum period.METHODSUsing claims data on all discharges from nonfederal emergency departments and acute care hospitals in California, we identified women who were hospitalized for labor and delivery between January 1, 2005, and June 30, 2010. We used validated diagnosis codes to identify a composite primary outcome of ischemic stroke, acute myocardial infarction, or venous thromboembolism. We then used conditional logistic regression to assess each patient's likelihood of a first thrombotic event during sequential 6-week periods after delivery, as compared with the corresponding 6-week period 1 year later.RESULTSAmong the 1,687,930 women with a first recorded delivery, 1015 had a thrombotic event (248 cases of stroke, 47 cases of myocardial infarction, and 720 cases of venous thromboembolism) in the period of 1 year plus up to 24 weeks after delivery. The risk of primary thrombotic events was markedly higher within 6 weeks after delivery than in the same period 1 year later, with 411 events versus 38 events, for an absolute risk difference of 22.1 events (95% confidence interval [CI], 19.6 to 24.6) per 100,000 deliveries and an odds ratio of 10.8 (95% CI, 7.8 to 15.1). There was also a modest but significant increase in risk during the period of 7 to 12 weeks after delivery as compared with the same period 1 year later, with 95 versus 44 events, for an absolute risk difference of 3.0 events (95% CI, 1.6 to 4.5) per 100,000 deliveries and an odds ratio of 2.2 (95% CI, 1.5 to 3.1). Risks of thrombotic events were not significantly increased beyond the first 12 weeks after delivery.CONCLUSIONSAmong patients in our study, an elevated risk of thrombosis persisted until at least 12 weeks after delivery. However, the absolute increase in risk beyond 6 weeks after delivery was low. (Funded by the National Institute of Neurological Disorders and Stroke.).

Database: Medline

12. Thromboembolism risk following recurrent miscarriage

Author(s): Martinez-Zamora M.A.; Balasch J.; Cervera R.

Source: Expert Review of Cardiovascular Therapy; 2013; vol. 11 (no. 11); p. 1503-1513

Publication Date: 2013

Publication Type(s): Review

PubMedID: 24134441

Available in full text at Expert Review of Cardiovascular Therapy - from ProQuest

Abstract: Normal pregnancy is associated with extensive changes in hemostasis such that the procoagulant effect becomes dominant. The evolutionary advantage of this hypercoagulability may be to counteract the inherent instability associated with hemochorial placentation, which is unique to human beings. However, overall, there is a four- to 10-fold increased thrombotic risk throughout gestation and the postpartum period. Certain inherited or acquired thrombophilic factors may predispose to arterial and/or venous thrombosis and have a possible association with pregnancy complications, including recurrent miscarriage (RM), which affects up to 5% of couples with childbearing desire. A subgroup of women with RM has been demonstrated to be in a prothombotic state before and after pregnancy. The long-term health implications of this hypercoagulability may imply an increased risk of ischemic heart disease. Moreover, the presence of antiphospholipid antibodies rather than thrombophilic genetic defects (i.e., factor V Leiden or prothrombin G202010A mutation) in patients with RM is a determinant of thrombotic events later in life, especially among those patients having also cardiovascular risk factors. This article highlights the thromboembolic risk in nonpregnant RM patients in different thrombophilic settings and the need for thromboprophylaxis among these patients. © 2013 Informa UK Ltd.

Database: EMBASE

13. Change of the initiation time of blood coagulation in pregnancy from 10-months to postpartum

Author(s): Sagesaka T.; Funabashi H.

Source: Clinical Hemorheology and Microcirculation; 2013; vol. 53 (no. 3); p. 247-255

Publication Date: 2013

Publication Type(s): Article

PubMedID: 22475689

Abstract: We measured the time of initiation of blood coagulation (Ti) from pregnancy 10-months (36~40 weeks) till 1-month after delivery, paying particular attention to the very early postpartum period, using a damped oscillation rheometer that is approximately 160 times more sensitive than the Thromboelastogram to evaluate the risk of thrombus formation. Blood samples were obtained from healthy volunteers at pregnancy 10-month, 1-hour, 3-hours, 4-days, 7-days, 3-weeks and 1-month after delivery. Ti values at pregnancy 10-month, 1-hour, 3-hours, 4-days, 7-days, 3-weeks, 1-month after delivery and in non-pregnant females were 20.4 +/- 2.2, 11.7 +/- 1.6, 13.2 +/- 3.1, 17.2 +/- 2.0, 20.2 +/- 1.6, 21.4 +/- 4.0, 24.6 +/- 3.6, and (25.0 +/- 3.4) minutes, respectively. Ti was significantly shorter at pregnancy 10-month, 1-hour, 3-ours, 4-days, 7-days and 3-weeks after delivery than in non-pregnant females. These data show that the blood of pregnant females is more hypercoagulable than non-pregnant females from pregnancy 10-month until 3-weeks post delivery, suggesting that they are at high risk of VTE after discharge from hospital. © 2013 - IOS Press and the authors.

Database: EMBASE

14. Platelet reactivity changes significantly throughout all trimesters of pregnancy compared with the nonpregnant state: A prospective study

Author(s): Burke N.; Flood K.; Murray A.; Cotter B.; Dempsey M.; Geary M.P.; Malone F.D.; Fay L.; Dicker P.; Kenny D.

Source: BJOG: An International Journal of Obstetrics and Gynaecology; Dec 2013; vol. 120 (no. 13); p. 1599-1604

Publication Date: Dec 2013

Publication Type(s): Article

PubMedID: 23924249

Abstract: Objective Platelets play an important role in the pathophysiology of uteroplacental disease and platelet reactivity may be an important marker of uteroplacental disease activity. However, platelet reactivity has not been evaluated comprehensively in normal pregnancy. We sought to evaluate platelet reactivity using a number of agonists at defined time points in pregnancy using a novel platelet assay and compare these with a nonpregnant cohort. Design Prospective longitudinal study. Setting Outpatient department of a large tertiary referral centre. Sample Eighty participants with 30 nonpregnant women and 50 pregnant women assessed longitudinally. Methods This was a prospective cohort study performed longitudinally throughout uncomplicated singleton pregnancies with participants recruited before 15 weeks of gestation. They were controlled for a number of factors known to affect platelet reactivity. Blood samples were obtained in each trimester. Thirty nonpregnant healthy female volunteers also had a platelet assay performed. A modification of standard light transmission aggregometry was used to assess platelet function, with light absorbance measured following the addition of five different agonists at submaximal concentrations. Dose-response curves were plotted for each agonist for the nonpregnant cohort and in each trimester for the pregnant cohort. Main outcome measures Dose-response curves and median effective concentration. Results When compared with the nonpregnant controls a significant reduction was demonstrated in platelet reactivity to collagen during the first trimester of pregnancy ($P < 0.0001$). Platelet aggregation increased significantly from the first to third trimesters in response to collagen and arachidonic acid. Conclusion Platelet reactivity varies according to pregnancy state, gestational age and agonist. The finding that platelet reactivity is reduced in the first trimester of pregnancy may be useful for the interpretation of further studies examining the role of platelet reactivity in the first trimester of pregnancies that develop uteroplacental disease. © 2013 RCOG.

Database: EMBASE

15. Molecular basis of type I antithrombin deficiency in two women with recurrent venous thromboembolism in the first trimester of pregnancy

Author(s): Xia Y.; Ding Q.; Wang X.; Lu Y.; Dai J.

Source: Journal of Thrombosis and Haemostasis; Dec 2013; vol. 11 ; p. 93

Publication Date: Dec 2013

Publication Type(s): Conference Abstract

Abstract: Objectives: Inherited antithrombin (AT) deficiency carries a 50% risk of venous thromboembolism (VTE) during pregnancy. Here, we investigated the molecular basis of type I AT deficiency in two women with recurrent VTE in the first trimester of pregnancy. Methods: Polymerase chain reaction (PCR)[A1] amplification of all exons and intron-exon junction regions of AT gene, followed by direct sequencing, was performed for the probands. In vitro expression experiments were performed in HEK293 or CHO cells transfected with either wild-type (WT) or mutant AT expression vectors. AT concentrations in the media and cell lysates were assayed by ELISA and western blot analysis. Intracellular localization of AT proteins was detected by immunofluorescence analysis. [A1]Although PCR is a commonly used abbreviation, please consider expanding it in the abstract. Results: Two novel heterozygous AT mutations were identified: g.7920 C>T resulting in a missense mutation (Trp225Cys) in case 1 and g.13863C>A causing an Ala404Asp mutation in case 2. In vitro levels of AT:Ag in Trp225Cys and Ala404Asp mutants were 4.8 +/- 0.4% and 7.9 +/- 0.6% of the AT-WT levels in the media, and 123.3 +/- 3.9% and 65.6 +/- 2.8% in cell lysates[A1], respectively. Immunofluorescence analysis revealed that the staining of AT-Trp225Cys in both endoplasmic reticulum (ER) and Golgi apparatus was similar to that of ATWT, and the staining of AT-Ala404Asp was mainly present in ER and was weaker than that of AT-WT. [A1]Please check if my revision conveys the intended meaning. Conclusion: The type I AT deficiency in two patients was caused by impaired secretion of the AT-Trp225Cys and AT-Ala404Asp mutant proteins, respectively. The two mutations are associated with a high risk of thrombotic onset and women with these AT mutations are prone to VTE in early pregnancy.

Database: EMBASE

16. Coagulation and fibrinolytic indices during the first trimester of pregnancy in women with polycystic ovary syndrome: a preliminary study.

Author(s): Shan, Yu; Wang, Aiming; Sun, Ying; Jiang, Wen; Pang, Baosen; An, Zhiyuan; Du, Xin; Wang, Wei; Huang, Zhongwei

Source: Reproductive sciences (Thousand Oaks, Calif.); Nov 2013; vol. 20 (no. 11); p. 1390-1397

Publication Date: Nov 2013

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 23585337

Abstract:OBJECTIVETo evaluate the levels of coagulation and fibrinolytic markers during the first trimester of pregnancy in women with polycystic ovary syndrome (PCOS) and determine the effects of PCOS and obesity on the levels of these hemostatic markers.METHODS A cross-sectional study was conducted in Beijing, China, on women with PCOS (n = 50), healthy women (n = 50), pregnant women with PCOS (n = 50), and healthy pregnant women (n = 50) at 12 weeks of pregnancy. Coagulation and fibrinolytic parameters were measured.RESULTSThe interaction between PCOS and pregnancy appears to exert effects on the activities of coagulation factors VIII and X. The interaction between PCOS and obesity also seems to affect the level of von Willebrand factor.CONCLUSIONSPregnant women with PCOS, especially women who are obese, are observed to be in a more prohemostatic state during the first trimester.

Database: Medline

17. Venous thromboembolism in pregnancy and the puerperal period: a study of 1210 events.

Author(s): Virkus, Rie Adser; Løkkegaard, Ellen C L; Lidegaard, Øjvind; Langhoff-Roos, Jens; Bjerregaard, Lars; Skovlund, Charlotte W; Bergholt, Thomas

Source: Acta obstetricia et gynecologica Scandinavica; Oct 2013; vol. 92 (no. 10); p. 1135-1142

Publication Date: Oct 2013

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article Evaluation Studies

PubMedID: 23869667

Abstract:OBJECTIVEThe aim of this study was to describe venous thromboembolism (VTE) in pregnancy and the puerperal period, and to validate diagnoses of VTE.DESIGNHistorical cohort study.POPULATIONAll pregnancies in Denmark from 1995 to 2009.METHODSVTE diagnoses were retrieved from national registries.MAIN OUTCOME MEASURESPositive predictive value of a VTE diagnoses diagnosed during pregnancy or the puerperal period. Location of VTE. Incidence rate of confirmed, validated diagnoses of VTE and on all retrieved diagnoses of VTE.RESULTSIn 1 297 037 pregnancies, 1436 women had a first-ever VTE diagnosis. Hospital records were retrieved for 1210 women (84.3%). Almost all women had relevant clinical symptoms and in 796 (65.8%), the diagnosis were confirmed by a positive diagnostic test or by instituted anticoagulation treatment. In all, 72.6, 53.7, 58.5 and 79.1% of the diagnoses were confirmed in the first, second, third trimester and the puerperal period, respectively. The 796 cases of VTE included 624 women with deep venous thrombosis only and 133 with pulmonary embolisms. Deep venous thrombosis was located in the left lower limb in 83.8% in pregnancy, compared with 67.9% in the puerperal period.CONCLUSIONSThe vast majority of women with a registered diagnosis of VTE had relevant symptoms. Diagnoses of VTE were confirmed in the medical records in two of three women. VTE diagnoses were most often confirmed when made in the first trimester and in the puerperal period. Left-sided deep venous thrombosis was the predominant type of VTE in pregnancy and the puerperal period.

Database: Medline

18. Prevalence of hereditary thrombophilia is the highest in women who developed pregnancy related thrombosis during first trimester

Author(s): Bodrozic J.; Miljic P.; Gojnic M.; Djordjevic V.

Source: Journal of Thrombosis and Haemostasis; Jul 2013; vol. 11 ; p. 867-868

Publication Date: Jul 2013

Publication Type(s): Conference Abstract

Available in full text at Journal of Thrombosis and Haemostasis - from John Wiley and Sons

Abstract: Background: Venous thrombosis is one of the leading causes of maternal morbidity and mortality. In women of reproductive age, over half of all venous thrombotic events are related to pregnancy and puerperium. Aims: We evaluated the presence of hereditary thrombophilia in women with thromboembolic complications during pregnancy and puerperium. Methods: We conducted a retrospective analysis of 143 consecutive women that developed thromboembolic complications during pregnancy or puerperium (6 weeks after the delivery), and who were referred to our institution for thrombophilia testing from January 2004 to October 2012. Venous thromboembolism was defined as deep vein thrombosis (DVT) of upper or lower extremities, cerebral vein thrombosis and pulmonary embolus (PE). When deep vein thrombosis of lower extremities was present with PE, the event was accounted as PE. Women with thrombosis of superficial veins were excluded from this study. All episodes of venous thromboembolism were confirmed with objective methods (duplex ultrasonography, CT angiography, perfusion scintigraphy, NMR angiography). In all women following causes of hereditary thrombophilia were tested: factor V Leiden and prothrombin G20210A mutations, antithrombin deficiency, protein C deficiency and protein S deficiency. Blood for thrombophilia testing was obtained at least 3 months after cessation of anticoagulant therapy. Results: Out of 143 women with pregnancy related thrombosis, 54 (38%) developed thromboembolic complications during pregnancy and 89 (62%) during puerperium. The presence of congenital thrombophilia was detected in 29 (54%) women who developed thrombosis during pregnancy and in 23 (46%) women with thromboembolic complications during puerperium. Out of 54 women who developed thrombosis during pregnancy, 15 (28%) had thromboembolic event in the first trimester of pregnancy, 11 (20%) in the second and 28 (52%) in the third, respectively. Prevalence of hereditary thrombophilia among women with thrombosis in the first, second and third trimester of pregnancy was 72%, 50% and 53%, respectively. In women who developed thrombosis during pregnancy distribution of thrombosis according localization was as follows: proximal vein thrombosis of lower extremities in 38 (70%), distal veins in 8 (16%), PE in 5 (9%), cerebral vein thrombosis in 2 (4%) and subclavio-axillaris thrombosis in 1(1%). On the other hand, in women with occurrence of thrombosis during puerperium was: proximal vein thrombosis in 42 (47%), distal vein in 21 (23%), PE in 17 (19%), ccerebral vein thrombosis in 8 (10%), subclavio axillar thrombosis in 1(1%). Summary/Conclusions: We observed the highest prevalence of hereditary thrombophilia in women who developed thrombosis during first trimester of pregnancy compared to advanced stages of pregnancy or puerperium. This finding may indicate the importance of acquired factors in occurrence of thrombosis in second and third trimester of pregnancy and during puerperium. Recognition and elimination of these factors may play an important role in prevention of pregnancy related thrombosis. Two times higher prevalence of PE in puerperium than during pregnancy may be a consequence of underdiagnosing this complication (reluctance to use CT angiography or perfusion scintigraphy) during pregnancy although we cannot exclude the real difference in prevalence of thrombosis during puerperium and during pregnancy.

Database: EMBASE

19. Platelet function is significantly reduced in the first trimester of pregnancy compared to the non-pregnant state

Author(s): Burke N.; Flood K.; Murray A.; Dempsey M.; Geary M.; Malone F.; Kenny D.; Dicker P.

Source: Archives of Disease in Childhood: Fetal and Neonatal Edition; Apr 2013; vol. 98

Publication Date: Apr 2013

Publication Type(s): Conference Abstract

Available in full text at Fetal and Neonatal - from BMJ Journals The NHS Collection

Abstract: Abnormalities of platelet function have been implicated in a number of obstetric complications and anti platelet therapy is used to prevent certain conditions. Research of platelet function in pregnancy has yielded conflicting results. We sought to critically evaluate platelet reactivity in pregnancy using an assay which allowed several agonists of varying concentrations to be assessed concurrently and aimed to clarify platelet reactivity in normal pregnancy. A prospective longitudinal study was performed throughout uncomplicated singleton pregnancies with patients recruited prior to 15 weeks' gestation. They were controlled for a number of factors known to affect platelet reactivity. Blood samples were obtained in each trimester (n = 36). Thirty non-pregnant healthy female volunteers also had a platelet assay performed. A modification of standard light transmission aggregometry was used to assess platelet reactivity, with light absorbance measured following addition of 5 different agonists at sub-maximal concentrations. Dose-response curves were plotted and the Ec50 was calculated for each agonist. Platelet reactivity, as demonstrated by the Ec50, was significantly reduced in the 1st and 2nd trimester of pregnancy compared to the non pregnant state particularly with respect to collagen, (p = 0.002). Within the pregnancy cohort the platelet reactivity increased as the pregnancy progressed, most evident in response to arachidonic acid (AA) (p = 0.033). This study demonstrates that platelet reactivity is altered in pregnancy, highlighted by the significant reduction in reactivity seen in the 1st trimester. This information will be critically important for designing and interpreting interventions to prevent obstetric complications, such as preeclampsia.

Database: EMBASE

20. Venous thromboembolism in pregnancy and the puerperal period. A study of 1,210 events in Denmark 1995.2009

Author(s): Virkus R.; Lokkegaard E.C.; Bergholt T.; Lidegaard O.; Skovlund C.; Langhoff-Roos J.; Bjerregaard L.

Source: Acta Obstetricia et Gynecologica Scandinavica; Jun 2012; vol. 91 ; p. 142

Publication Date: Jun 2012

Publication Type(s): Conference Abstract

Available in full text at Acta Obstetricia et Gynecologica Scandinavica - from John Wiley and Sons

Abstract: Introduction: The aim of this study was to describe venous thromboembolism (VTE) in pregnancy and the puerperal period and to validate ICD-10 diagnoses of VTE. Material and methods: Historical cohort study including all pregnancies in Denmark from 1995 to 2009. VTE diagnoses were retrieved from the National Registry of Patients. Results: In 1,377,286 pregnancies, 1,436 women had a first ever VTE diagnosis.Hospital records were retrieved for 1,210 women (84.3%). Most women had relevant clinical symptoms, and 796 (65.8%) were considered confirmed by a positive diagnostic test or instituted anticoagulation treatment. In all, 72.6%, 53.7%, 58.5% and 79.1% of the diagnoses were confirmed in the first, second, and third trimester, and the puerperal period, respectively. The incidence rate of confirmed VTE was 0.7 per 1,000 pregnancies. The 796 confirmed diagnoses of VTE included 624 women with deep venous thrombosis only, 133 with pulmonary

embolism, of which 27 also had deep venous thrombosis. During pregnancy, deep venous thrombosis was located in the left lower limb in 83.8%, compared to 67.9% in the puerperal period. The mean number of days with clinical symptoms before admission with deep vein thromboses and pulmonary embolism was 5.8 days and 8.0 days, respectively. Of the 654 confirmed events of deep vein thrombosis, 586 (89.6%) were diagnosed by Doppler ultrasound or phlebography. Of 133 pulmonary embolism, 109 (82.0%) were confirmed by pulmonary scintigraphy or CT-scan. Of the confirmed deep venous thrombosis the proportion with a positive diagnostic test rose from 87.7% in pregnancy to 97.2% in the puerperal period. Conclusions: Almost all women diagnosed with VTE had relevant symptoms. Diagnoses of VTE were paraclinically confirmed in 2 out of 3 women. The validity of diagnoses of VTE was highest during the first trimester and in the puerperal period.

Database: EMBASE

21. Changes in coagulation and hemodynamics during pregnancy: a prospective longitudinal study of 58 cases.

Author(s): Hui, Chen; Lili, Meng; Libin, Chen; Rui, Zhang; Fang, Guo; Ling, Gao; Jianping, Zhang

Source: Archives of gynecology and obstetrics; May 2012; vol. 285 (no. 5); p. 1231-1236

Publication Date: May 2012

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 22083312

Available in full text at Archives of Gynecology and Obstetrics - from Springer Link Journals

Abstract:PURPOSETo investigate changes and establish reference values in coagulation, anticoagulation, fibrinolysis, anti-fibrinolysis and hemodynamics during normal pregnancy.METHODSA total of 58 women with singleton pregnancies were recruited. Blood and ultrasound examinations were performed in the 10th-14th, 20th-24th, and 30th-34th weeks of pregnancy. The same examinations were performed in 50 non-pregnant women who were selected as the control group.RESULTSLevels of fibrinogen, thrombin time, fibronectin, prothrombin activated fragments 1+2 and thrombomodulin were higher in early pregnancy than those in the control group ($P < 0.05$). Fibrinogen, prothrombin time, activated partial thromboplastin time, thrombin time, thromboxane B2, prothrombin activated fragments 1+2, thrombomodulin, D-dimer, and plasminogen activator inhibitor-2 were statistically different between the mid pregnancy and the control group ($P < 0.05$). Meanwhile, fibrinogen, prothrombin time, activated partial thromboplastin time, thrombin time, fibronectin, thromboxane B2, prothrombin activated fragments 1+2, thrombomodulin, and plasminogen activator inhibitor-2 were obviously elevated in late pregnancy as compared with the control group ($P < 0.05$). Moreover, fibrinogen, thromboxane B2, prothrombin activated fragment 1+2, D-dimer plasminogen, and activator inhibitor-2 gradually increased during pregnancy with some fluctuation. Prothrombin time, activated partial thromboplastin time, thrombin time, international normalized ratio, and thrombomodulin as well as systolic/diastolic ratio, pulsatility index, and resistance index in uterine arteries showed a tendency to decrease in pregnant women.CONCLUSIONSCoagulation, anti-coagulation, fibrinolytic and anti-fibrinolytic activities are enhanced and balanced at a higher level during pregnancy. In addition, uterine artery and umbilical artery hemodynamics become more baby friendly (i.e., high flow and low resistance).

Database: Medline

22. Changes in thrombin generation during pregnancy as measured by computerized automated thrombography (CAT)

Author(s): Shah N.R.; Ortel T.; Thames E.; James A.H.

Source: American Journal of Hematology; May 2012; vol. 87

Publication Date: May 2012

Publication Type(s): Conference Abstract

Available in full text at American Journal of Hematology - from John Wiley and Sons

Abstract: Background: Normal pregnancy is associated with a hypercoagulable state secondary to various changes in coagulation factors, including fibrinogen and thrombin. Global assays such as CAT can be used to reflect thrombin generation and display the phases of thrombin generation including lag phase (LT), acceleration phase, peak, and endogenous thrombin potential (ETP). Objective: To describe thrombin generation longitudinally in pregnancy using the CAT global assay. Methods: We performed a prospective cohort study of 125 pregnant females who were >=18 years. Women with multiple gestations were excluded. Blood was drawn initially between 12 and 14 weeks (end of first trimester), subsequently between 24 and 28 weeks gestation (end of second trimester), and finally at 6 weeks postpartum (baseline). Thrombin generation was measured by use of CAT (Stago Diagnostica). Mean values were compared using a twosided t-test. Results: LT and acceleration phase during 12-14 weeks were nonsignificantly shorter than 24-28 weeks (4.13 +/- 0.16 vs. 4.6 +/- 0.19, P = 0.06 and 6.49 +/- 0.22 vs. 6.88 +/- 0.24, P = 0.24, respectively). ETP and peak during 12-14 weeks were also not significantly different than 24-28 weeks. Mean values of all phases of CAT during 12-14 weeks were significantly different than 6 weeks postpartum including ETP (1,814 +/- 46 vs. 1,234 +/- 41; P < 0.0001) and peak (350.6 +/- 11.63 vs. 218 +/- 10.7; P < 0.0001). CAT was also significantly different during 24-28 weeks gestation when compared with 6 weeks postpartum, including ETP (1,837 +/- 55 vs. 1,234 +/- 41; P < 0.0001) and peak (359 +/- 10.66 vs. 218 +/- 10.7; P < 0.0001). Conclusions: Although we found no significant difference in thrombin generation between 12-14 weeks and 24-28 weeks gestation, we did document a significant difference during pregnancy when compared with 6 weeks postpartum (baseline).

Database: EMBASE

23. Coagulation and prothrombotic state parameters: a clinical analysis during early pregnancy.

Author(s): Chen, H; Zhou, L; Meng, L; Liu, M; Tan, J; Gao, L; Zhang, J

Source: Irish journal of medical science; Dec 2011; vol. 180 (no. 4); p. 813-817

Publication Date: Dec 2011

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 21809018

Available in full text at Irish Journal of Medical Science - from Springer Link Journals

Abstract:AIMThe aim of this study is to assess the changes in coagulation, thrombosis, anticoagulation, and fibrinolysis during early pregnancy.METHODSOne hundred and five pregnant women with monozygotic pregnancies between 10 and 12 weeks gestation were randomly enrolled as the study group, and another 82 non-pregnant women were selected as the control group. Coagulation parameters and prothrombotic state parameters were measured.RESULTSFg, F1 + 2, thrombin-antithrombin complex, GMP140, D-dimer, and plasminogen activator inhibitor 2 were statistically different between the study and the control groups ($p < 0.008$). The coagulation, fibrinolytic, and the antifibrinolytic functions of healthy pregnant women are enhanced during early pregnancy, whereas the anticoagulation is slightly increased.CONCLUSIONCoagulation, fibrinolysis, and antifibrinolysis remain at high levels, whereas the platelet activation remains at low levels during early pregnancy.

Database: Medline

24. The hemostatic system with medical abortion

Author(s): Vorobyeva N.A.; Nemanova S.B.

Source: Thrombosis Research; Feb 2011; vol. 127

Publication Date: Feb 2011

Publication Type(s): Conference Abstract

Abstract: An alternative to surgical methods of abortion is a pharmacological abortion. Materials and Methods: The evaluation of the hemostatic system in 65 women on the background of medical abortion in early pregnancy, the combined use of drugs mifepristone and misoprostol. Results of the study: Average biochemical, hematological parameters and hemostasis coagulatory parameters before pharmacological abortion corresponded to the normal ranges for this age-sex group. To the 4th day of abortion statistically significant (p rd-4th day and its statistically significant (p rd-10th day of abortion. Plasminogen level tended to decrease (p = 0.081) to the 3rd-4th day of abortion comparatively to base level. a2-antiplasmin activity also declined (p rd-4th day. 19.23% D-dimer increase was shown to the 3rd-4th day of abortion. Conclusion: Our data show that in hemostasis system of pregnant woman in early term after pharmacological abortion significant changes of hemostasis parameters demanding laboratory control take place.

Database: EMBASE

25. Quality of hemostasis in women with missed abortion and miscarriages: The role of molecular and genetic thrombophylia factors

Author(s): Vasilenko I.; Ordijants I.; Vasina O.; Makaeva D.; Strizhova T.; Nalgieva M.

Source: Pathophysiology of Haemostasis and Thrombosis; 2010; vol. 37

Publication Date: 2010

Publication Type(s): Conference Abstract

Abstract: Background: One of the reasons of obstetric complications is development of hypercoagulation produced by different congenital and acquired thrombophilia factors. The changes in the coagulation and the fibrinolytic system which may be related to the early losses indicate an interference of the activation of both coagulation and fibrinolysis. During termination of missed abortion and missed labour disorders of the hemostasis may occur acutely. The aim of this study was to evaluate the role of hemostasis disruption in genesis of first- and second-trimester miscarriage. 75 pregnant women of reproductive age in dynamics were examined: 55 women with reproductive losses in the anamnesis and 20 healthy pregnants. We analyzed the following hemostasis parameters: prothrombin time (PT), partial thromboplastin time (PTT), D-dimer, fibrinogen, the soluble fibrin monomer complex (SFMC), plasminogen, von Willebrand factor antigen (vWFA) by "Sta compact" (Roche). Morphofunctional status of peripheral blood platelets we determined by real-time method of vital computer morphometry using computer coherent phase-interference microscope (CPM) "Cytoscan". Homocystein plasma levels were measured by polarization fluorescent immunoanalyzer. Gene mutation was studied by allelespecific polymerase chain reaction. It was determined that the damages of platelet hemostasis in reccurent miscarriage are consisted cell morphology and functional activity. We detected the frank heterogeneity of circulative platelet population which was connected to increasing quantity of macro-platelets with different image density. The 78% of patients had the high level of platelet activating state with failure of compensation (43%-the resting platelets; 41% - activating forms; 16% - degenerating forms).We registered the tendency to increasing of platelet aggregation. No essentiel changes in the plasmatic system of coagulation and fibrinolysis were found. The hemostasis disruptions induced the deficit of microcirculation, thrombosis of blood vessels, infarcts of placenta. Thus, we may conclude that practically more than 50% of early reproductive losses are connected to molecular and genetic thrombophilia factors.

Database: EMBASE

26. Platelet function in the first trimester

Author(s): Flood K.; Kent E.; Malone F.D.; Peace A.; Tedesco T.; Kenny D.; Dicker P.; Geary M.

Source: American Journal of Obstetrics and Gynecology; Dec 2009; vol. 201 (no. 6)

Publication Date: Dec 2009

Publication Type(s): Conference Abstract

Abstract:OBJECTIVE: To determine if platelet reactivity is altered in the first trimester of pregnancy. STUDY DESIGN: 10 healthy pregnant volunteers were recruited at time of first trimester screening (between 11-13 weeks gestation). Controls included 10 age-matched healthy subjects with prior good obstetric outcome. A 30 ml blood sample was taken and platelet function assessed using a novel assay of platelet reactivity. Platelet aggregation to multiple concentrations of Arachidonic Acid (AA), Collagen (Col), Epinephrine (Epi) and Adenosine-Diphosphate (ADP) were measured simultaneously over successive time-points using a modification of light transmission aggregometry. Dose-response curves were graphed with the maximum aggregatory response calculated to multiple doses of each agonist. RESULTS: The pregnant group were significantly less reactive to all submaximal doses of Epi: 1% versus 25% at dose 0.78 mcM, 5% versus 40% at dose 3.125mcM, 15%

versus 50% at dose 12.5 mcM, 38% versus 65% at dose 50mcM and 60% versus 76% at dose 200mcM with overall paired p value <0.01. The pregnant group were also less reactive to submaximal doses of AA: 11% versus 20% at dose 0.93mg/ml and 14% versus 35% at dose 1.875mg/ml (p<0.06) and submaximal doses of Coll: 48% versus 72% at dose 0.71 mg/ml and 68% versus 82% at dose 1.43mg/ml (p<0.06). The groups were similar in their aggregatory reponse to ADP. CONCLUSION: Increased platelet reactivity in pregnancy has been shown in numerous in vivo and in vitro studies, however, this effect has usually been demonstrated in the second and third trimesters. Using a novel platelet assay this study has demonstrated global platelet under-reactivity early in pregnancy which may represent an adaptive mechanism to allow successful implantation. Further studies are planned to evaluate the outcome of pregancies that do not follow this normal platelet functional response.

Database: EMBASE

27. Haemostatic changes in the puerperium '6 weeks postpartum' (HIP Study) - Implication for maternal thromboembolism

Author(s): Saha P.; Atalla R.; Stott D.

Source: BJOG: An International Journal of Obstetrics and Gynaecology; Nov 2009; vol. 116 (no. 12); p. 1602-1612

Publication Date: Nov 2009

Publication Type(s): Article

PubMedID: 19681851

Abstract: Objective We aim to measure the thrombotic changes during the postnatal period up to 6 weeks after delivery and assess the extent of the risk period. Design Prospective observational study. Setting Queen Elizabeth II, an acute District General Hospital, Hertfordshire. Population Women booked at the antenatal clinic and prepared to deliver at the hospital. Methods We assessed the haemoglobin, platelet count and function, fibrinogen, prothrombin time, activated partial thromboplastin time, protein C, S and antithrombin level and as well as rotational thromboelastometry (ROTEM) from predelivery till 6 weeks postpartum. Results A total 50 women were recruited of which four dropped out. Results compared against the finding at 6 weeks after delivery. Platelet was significantly elevated on day 19 compared to day 42 (P < 0.001). Fibrinogen was elevated from predelivery till day 15 after delivery (P < 0.01). Prothrombin time (PT) was low till day 15 (P < 0.05) and activated partial thromboplastin time (APTT) was significantly lower till day 3 after delivery (P < 0.001). ROTEM revealed low clotting time (CT) at predelivery and continued to be low till day 7. Clot formation time (CFT) significantly low till day 25 (P < 0.05). Maximum clot firmness, alpha angle and amplitude at 20 minutes were raised till day 19 (P < 0.001, P < 0.01 and P < 0.001 respectively). While, comparing vaginal delivery against caesarean section there were nonsignificant increase in thrombotic parameters in caesarean section. Conclusion Coagulation screens as well as thomboelastometry suggest a persistent hypercoagulation during the first 3 weeks after delivery. © RCOG 2009 BJOG An International Journal of Obstetrics and Gynaecology.

Database: EMBASE

28. Pregnancy, the postpartum period and prothrombotic defects: Risk of venous thrombosis in the MEGA study

Author(s): Pomp E.R.; Lenselink A.M.; Rosendaal F.R.; Doggen C.J.M.

Source: Journal of Thrombosis and Haemostasis; Apr 2008; vol. 6 (no. 4); p. 632-637

Publication Date: Apr 2008

Publication Type(s): Article

PubMedID: 18248600

Abstract: Background: Venous thrombosis is one of the leading causes of maternal morbidity and mortality. Objective: In the MEGA study, we evaluated pregnancy and the postpartum period as risk factors for venous thrombosis in 285 patients and 857 control subjects. Patients/methods: Between March 1999 and September 2004, consecutive patients with a first episode of venous thrombosis were included from six anticoagulation clinics. Partners of patients and a random digit dialing group were included as control subjects. Participants completed a questionnaire and DNA was collected. Results: The risk of venous thrombosis was 5-fold (OR, 4.6; 95% CI, 2.7-7.8) increased during pregnancy and 60-fold (OR, 60.1; 95% CI, 26.5-135.9) increased during the first 3 months after delivery compared with non-pregnant women. A 14-fold increased risk of deep venous thrombosis of the leg was found compared with a 6-fold increased risk of pulmonary embolism. The risk was highest in the third trimester of pregnancy (OR, 8.8; 95% CI, 4.5-17.3) and during the first 6weeks after delivery (OR, 84.0; 95% CI, 31.7-222.6). The risk of pregnancy-associated venous thrombosis was 52-fold increased in factor V Leiden carriers (OR, 52.2; 95% CI, 12.4-219.5) and 31-fold increased in carriers of the prothrombin 20210A mutation (OR, 30.7; 95% CI, 4.6-203.6) compared with non-pregnant women without the mutation. Conclusion: We found an increased risk of venous thrombosis during pregnancy and the postpartum period, with an especially high risk during the first 6weeks postpartum. The risk of pregnancy-associated venous thrombosis was highly increased in carriers of factor V Leiden or the prothrombin 20210A mutation. © 2008 International Society on Thrombosis and Haemostasis.

Database: EMBASE

29. Venous thromboembolism during pregnancy or postpartum: findings from the RIETE Registry.

Author(s): Blanco-Molina, Angeles; Trujillo-Santos, Javier; Criado, Juan; Lopez, Luciano; Lecumberri, Ramón; Gutierrez, Reyes; Monreal, Manuel; RIETE Investigators

Source: Thrombosis and haemostasis; Feb 2007; vol. 97 (no. 2); p. 186-190

Publication Date: Feb 2007

Publication Type(s): Research Support, Non-u.s. Gov't Comparative Study Multicenter Study Journal Article

PubMedID: 17264945

Abstract: Venous thromboembolism (VTE) occurs infrequently during pregnancy, and issues concerning its natural history, prevention and therapy remain unresolved. RIETE is an ongoing registry of consecutive patients with objectively confirmed, symptomatic acute VTE. In this analysis, we compared the clinical characteristics and outcome for all enrolled pregnant and postpartum women with acute VTE, and all non-pregnant women in the same age range. Up to May 2005, 11,630 patients were enrolled in RIETE, of whom 848 (7.3%) were women aged <47 years. Of them, 72 (8.5%) were pregnant, 64 (7.5%) postpartum. Pregnant women presented less often with symptomatic pulmonary embolism (11%) than non-pregnant women (39%). VTE developed during the first trimester in 29 (40%) pregnant patients; in the second in 13; in the third in 30. Thrombophilia tests were more often positive in women who had VTE during the first trimester (odds ratio [OR]: 4.4; 95% CI: 0.9-2.4; p=0.037). Most patients in all three groups were initially treated with low-molecular-weight heparin (LMWH). As for long-term therapy, 75% of pregnant women received LMWH until delivery. There were no maternal deaths, and no pregnant patient had recurrence or bled before delivery. However, after delivery one patient (1.4%) developed recurrent thrombosis, four (5.6%) had major bleeding. In conclusion, VTE developed during the first trimester in 40% of the pregnant women, thus suggesting that thromboprophylaxis, when indicated during pregnancy, should start in the first trimester. No patient showed recurrence or bled before delivery, but after delivery the risk of bleeding exceeded the risk of recurrences.

Database: Medline

30. Hemostasis during normal pregnancy and puerperium.

Author(s): Hellgren, Margareta

Source: Seminars in thrombosis and hemostasis; Apr 2003; vol. 29 (no. 2); p. 125-130

Publication Date: Apr 2003

Publication Type(s): Journal Article Review

PubMedID: 12709915

Abstract: During normal pregnancy the hemostatic balance changes in the direction of hypercoagulability, thus decreasing bleeding complications in connection with delivery. The most important initial factor for acute hemostasis at delivery is, however, uterine muscle contractions, which interrupt blood flow. Global tests such as Sonoclot signature, the Thromboelastogram, and a new method analyzing overall plasma hemostasis, all show changes representative of hypercoagulability during pregnancy. Increased endogenous thrombin generation, acquired activated protein C resistance, slightly decreased activated partial thromboplastin time (aPTT) and increased prothrombin complex level (PT) measured as international normalized ratio (INR) of less than 0.9 have been reported as well. In normal pregnancy, the platelet count is within normal range except during the third trimester when benign gestational thrombocytopenia, 80 to 150 x 10 9/L, can be observed. Platelet turnover is usually normal. Activation of platelets and release of beta-thromboglobulin and platelet factor 4 are reported. The bleeding time is unchanged during normal

pregnancy. Most blood coagulation factors and fibrinogen increase during pregnancy. Factor (F) XI is the only blood coagulation factor that decreases. Blood coagulation inhibitors are mainly unchanged but the level of free protein S decreases markedly and the level of tissue factor pathway inhibitor increases. Thrombomodulin levels increase during pregnancy. Fibrinolytic capacity is diminished during pregnancy, mainly because of markedly increased levels of plasminogen activator inhibitor-1 (PAI-1) from endothelial cells and plasminogen activator inhibitor-2 (PAI-2) from the placenta. Thrombin-activated fibrinolysis inhibitor is reported to be unaffected. The total hemostatic balance has been studied by analyses of prothrombin fragment 1+2, thrombin-antithrombin complex, fibrinopeptide A, soluble fibrin, D-dimer, and plasmin-antiplasmin complex. There is activation of blood coagulation and a simultaneous increase in fibrinolysis without signs of organ dysfunction during normal pregnancy. These changes increase as pregnancy progresses. During delivery, there is consumption of platelets and blood coagulation factors, including fibrinogen. Fibrinolysis improves and increases fast following childbirth and expulsion of the placenta, resulting in increased D-dimer levels. These changes are self-limiting at normal delivery. The hemostatic changes, noted during pregnancy, normalize after delivery within 4 to 6 weeks. Platelet count and free protein S, however, can be abnormal longer. Hemostasis should not be tested earlier than 3 months following delivery and after terminating lactation to rule out influences of pregnancy. PAI-1 and PAI-2 levels decrease fast postpartum, but PAI 2 has been detected up to 8 weeks postpartum. alpha 2 -antiplasmin, urokinase, and kallikrein inhibitor levels have been reported to be increased 6 weeks postpartum.

Database: Medline

31. PHYSIOLOGIC CHANGES IN COAGULATION AND FIBRINOLYSIS DURING NORMAL PREGNANCY

Author(s): Deitcher S.R.; Gardner J.F.

Source: Clinics in Liver Disease; Feb 1999; vol. 3 (no. 1); p. 83-96

Publication Date: Feb 1999

Publication Type(s): Article

Abstract: The human hemostatic system consists of multiple independent, yet integrally related, cellular and protein components that function to maintain blood fluidity under normal conditions and promote localized, temporary thrombus formation at sites of vascular injury. A normal hemostatic system is the human physiologic defense against exanguination. An abnormal hemostatic system can result in pathologic bleeding, vascular thrombosis, or both. The hemostatic system comprises of six major components: platelets, vascular endothelium, procoagulant plasma protein factors, natural anticoagulant proteins, fibrinolytic proteins, and antifibrinolytic proteins. Each of these six hemostatic components must be present in a fully functional form and in an adequate quantity to prevent excessive blood loss following vascular trauma and at the same time prevent pathologic thrombosis. The hemostatic system is highly regulated and maintains a delicate balance between a prohemorrhagic state and a prothrombotic state. Any significant acquired or congenital imbalance in the hemostatic scales can lead to a pathologic outcome. Alterations in the quantitative and qualatative status of any hemostatic cellular or protein element can have significant biologic effect. Platelet deficiency (thrombocytopenia), platelet adhesion defects, and platelet aggregation disorders are associated with an inability to form an adequate primary hemostatic platelet plug and can lead to significant mucocutaneous bleeding and post-traumatic, life-threatening hemorrhage. In contrast, a marked increase in platelet count (thrombocytosis) and accentuated platelet aggregation (sticky platelet syndrome) are associated with thromboembolic events.32 Deficiency of a procoagulant factor integral to the intrinsic (factors XI, IX, and VIII), extrinsic (factor VII), or common (factors X, V, II and fibrinogen) pathway of coagulation is associated typically with a variable degree of bleeding tendency. Elevated levels of procoagulant factors, such as factor VIII, fibrinogen, and factor VII, however, are recognized risk factors for vascular disease.28,47 Deficiency of natural anticoagulant proteins, such as protein C, protein S, antithrombin III (AT-III), and heparin cofactor II

(HC-II), is associated with venous thromboembolic disease; a natural anticoagulant protein excess state associated with bleeding has not been described to date.13 Deficiency of a fibrinolytic cascade component, such as tissue-type plasminogen activator (t-PA) or plasminogen; and excess plasma levels of the fibrinolytic inhibitor, plasminogen activator inhibitor-1 (PAI-1), have been linked to hypercoagulability and thrombosis.24,29,53 Deficiency of fibrinolytic inhibitors, such as alpha-2 antiplasmin and PAI-1, may precipitate a hyperfibrinolytic bleeding state.30,52 Deficiency of endothelial cell-derived von Willebrand factor is associated with altered primary and secondary hemostasis caused by deficient platelet anchoring at sites of vascular injury and shortened factor VIII survival characteristic of von Willebrand's disease.20 Deficient endothelial cell production of thrombomodulin or release of t-PA may be associated with a thrombotic tendency.19 The balance between these opposing groups of proteins and not the level of any individual factor seems most critical to hemostatic regulation. Pregnant women differ from nonpregnant adults in many physiologic and biochemical aspects. Normal pregnancy is associated with major changes in the coagulation and fibrinolytic systems. The many hemostatic derrangements detected during pregnancy must be considered to represent physiologic, adaptive, and preparatory mechanisms for the hemostatic challenges of delivery rather than pathologic processes. Most pregnant women do not manifest overt bleeding nor thrombotic problems. The hemostatic changes observed in each trimester of normal pregnancy and the puerperium reflect diverse changes in coagulation factor, fibrinolytic protein, regulatory protein, and cellular component activation, release, consumption, and synthesis. The fact that most hemostatic factors and proteins are liver derived, makes a review of coagulation alterations in pregnancy an appropriate component of an article on the liver and pregnancy. This article focuses on all hemostatic components involved in primary hemostasis (platelet plug formation) and secondary hemostasis (fibrin mesh formation) as well as the mechanisms responsible for thrombus localization (natural anticoagulants) and ultimate removal (fibrinolytic cascade proteins). The effects of each trimester of normal pregnancy and the puerperium on each of the major components of the hemostatic system are examined. Particular attention is paid to the balance between procoagulant and anticoagulant mechanisms and the net effect of the hemostatic changes at different periods during pregnancy.

Database: EMBASE

32. Fibrinolysis changes in normal pregnancy.

Author(s): Bellart, J; Gilabert, R; Fontcuberta, J; Borrell, M; Miralles, R M; Cabero, L

Source: Journal of perinatal medicine; 1997; vol. 25 (no. 4); p. 368-372

Publication Date: 1997

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 9350608

Abstract: The aim of this study was to evaluate the changes in fibrinolysis parameters during pregnancy. Normal pregnant women (n = 60) formed the study population. Blood samples were taken in the first, second and third trimester, during delivery and three days after delivery. Fibrinolysis parameters were estimated using commercial tests. Tissue plasminogen activator, D-dimer and plasminogen activator inhibitors (PAI-1 and PAI-2) were determined. Tissue plasminogen activator and D-dimer increased after the first trimester and reached maximum levels during delivery. Plasminogen activator inhibitors type 1 and type 2 were also higher, in particular PAI-2, and reached maximum levels in the third trimester. On the third day after delivery, fibrinolysis activity recovered, but D-dimer and PAI-2 levels remained above the normal non-pregnant range.

Database: Medline

33. Coagulation factors in women using oral contraceptives or intrauterine contraceptive devices immediately after abortion.

Author(s): Lähteenmäki, P; Rasi, V; Luukkainen, T; Myllyä, G

Source: American journal of obstetrics and gynecology; Sep 1981; vol. 141 (no. 2); p. 175-179

Publication Date: Sep 1981

Publication Type(s): Research Support, Non-u.s. Gov't Journal Article

PubMedID: 6792922

Abstract: The changes in coagulation parameters were studied in 24 women who started using microdose combined oral contraceptives immediately after first-trimester abortion. Another 24 women who had an intrauterine contraceptive device inserted at the end of the abortion procedure were studied as control subjects. In pill users, a slightly increaed tendency toward hypercoagulability was observed 1 week after abortion in terms of elevated fibrinogen and Factor VIII as well as decreased antithrombin levels. Other studies have shown that the new follicle development after first-trimester abortion starts beyond the first week. It would therefore seem that by postponing oral contraceptive use until 1 week after abortion, no decrease in the effectiveness of contraception occurs and the possible risks of hypercoagulabilty during the postabortal period can be avoided.

Database: Medline

Strategy 264940

#	Database	Search term	Results
1	Medline	("venous thromboemboli*").ti,ab	17862
2	Medline	exp "VENOUS THROMBOEMBOLISM"/	7385
3	Medline	(1 OR 2)	19212
4	Medline	(first ADJ2 trimester*).ti,ab	21161
5	Medline	(1st ADJ2 trimester*).ti,ab	842
6	Medline	exp "PREGNANCY TRIMESTER, FIRST"/	14769
7	Medline	(earl* ADJ2 pregna*).ti,ab	22649
8	Medline	(4 OR 5 OR 6 OR 7)	46338
9	Medline	(3 AND 8)	109
10	Medline	(hypercoagul*).ti,ab	5098
11	Medline	(8 AND 10)	48
12	Medline	(early ADJ2 abortion*).ti,ab	1517
13	Medline	(early ADJ2 miscarriage*).ti,ab	499
14	Medline	(12 OR 13)	2001
15	Medline	(10 AND 14)	5
16	Medline	exp "ABORTION, SPONTANEOUS"/	35838
17	Medline	(10 AND 16)	38
18	Medline	exp "PREGNANCY, ECTOPIC"/	13904
19	Medline	(ectopic ADJ2 pregn*).ti,ab	8116

20	Medline	(18 OR 19)	16079
21	Medline	(10 AND 20)	1
22	Medline	(3 AND 20)	4
23	Medline	exp "ABORTION, INDUCED"/	37962
24	Medline	(3 AND 23)	10
25	Medline	(10 AND 23)	4
26	Medline	exp "BLOOD COAGULATION"/	54966
27	Medline	(8 AND 26)	82
28	Medline	(prothrombo*).ti,ab	5076
29	Medline	(8 AND 28)	24
30	Medline	(14 AND 28)	0
31	Medline	(20 AND 28)	0
32	Medline	(23 AND 28)	0
33	Medline	(fibrinoly*).ti,ab	30997
34	Medline	(8 AND 33)	77
35	EMBASE	*"FIRST TRIMESTER PREGNANCY"/	9077
36	EMBASE	*"VENOUS THROMBOEMBOLISM"/	12813
37	EMBASE	(35 AND 36)	3
38	EMBASE	exp HYPERCOAGULABILITY/	9321
39	EMBASE	(hypercoagul*).ti,ab	12315
40	EMBASE	(38 OR 39)	16352

41	EMBASE	(35 AND 40)	11
42	EMBASE	(prothrombo*).ti,ab	7860
43	EMBASE	(35 AND 42)	5
44	EMBASE	*"BLOOD CLOTTING"/	26070
45	EMBASE	(35 AND 44)	3
46	EMBASE	*"SPONTANEOUS ABORTION"/	11555
47	EMBASE	(40 AND 46)	47
48	EMBASE	(36 AND 46)	0
49	EMBASE	("venous thromboemboli*").ti,ab	27972
50	EMBASE	exp "VENOUS THROMBOEMBOLISM"/	127875
51	EMBASE	(49 OR 50)	0
52	EMBASE	(46 AND 51)	42
53	EMBASE	exp "FIRST TRIMESTER PREGNANCY"/	33707
54	EMBASE	(36 AND 53)	30
55	EMBASE	(39 AND 46)	33
56	EMBASE	exp "INDUCED ABORTION"/	33925
57	EMBASE	(36 AND 56)	3
58	EMBASE	(40 AND 56)	18
59	EMBASE	(40 AND 53)	74
60	EMBASE	exp FIBRINOLYSIS/	68496
61	EMBASE	(56 AND 60)	41

62	EMBASE	(44 AND 56)	41
63	EMBASE	(53 AND 60)	68
64	EMBASE	exp "ECTOPIC PREGNANCY"/	18961
65	EMBASE	(60 AND 64)	10
66	EMBASE	(44 AND 64)	13
67	EMBASE	(51 AND 64)	147
68	EMBASE	(36 AND 64)	2
69	EMBASE	(40 AND 56)	18
70	EMBASE	exp "BLOOD CLOTTING"/	203349
71	EMBASE	(35 AND 70)	47
72	EMBASE	(46 AND 70)	123
73	EMBASE	(42 AND 56)	1
74	EMBASE	(hypercoagul* ADJ3 persist*).ti,ab	83
75	EMBASE	(pregn*).ti,ab	563672
76	EMBASE	(74 AND 75)	5
77	EMBASE	(FIBRINOLy* ADJ3 PERSIST*).ti,ab	52
78	EMBASE	(75 AND 77)	1
79	EMBASE	(64 AND 70)	101
80	EMBASE	exp "ANTICOAGULANT AGENT"/	592648
81	EMBASE	(56 AND 80)	269
83	EMBASE	("pro thromboemb*").ti,ab	3

84	EMBASE	exp "THROMBOCYTE FUNCTION"/	84483
85	EMBASE	(53 AND 84)	64
86	EMBASE	(56 AND 84)	17
87	EMBASE	(53 AND 84)	64
88	EMBASE	(64 AND 84)	7
89	Medline	exp "BLOOD COAGULATION FACTORS"/	447855
90	Medline	(8 AND 89)	621
91	Medline	(hypercoagulation OR hypercoagulability).ti,ab	4478
92	Medline	(8 AND 91)	33
93	EMBASE	(postabort*).ti,ab	1085
94	EMBASE	(84 AND 93)	0
95	EMBASE	(70 AND 93)	8
96	EMBASE	(abortion ADJ2 haemostasis).ti,ab	0
97	EMBASE	(abortion ADJ2 hemostasis).ti,ab	2
98	EMBASE	(miscarriage* ADJ2 hemostasis).ti,ab	0
99	EMBASE	(miscarriage* ADJ2 haemostasis).ti,ab	0
101	EMBASE	exp "SPONTANEOUS ABORTION"/co,si	3934
102	EMBASE	(70 AND 101)	59
103	EMBASE	(51 AND 101)	153

104	EMBASE	(pregn* ADJ2 termin*).ti,ab	14413
105	EMBASE	(51 AND 104)	69
106	EMBASE	*"ANTICOAGULANT AGENT"/	34013
107	EMBASE	(46 AND 106)	25
108	EMBASE	(56 AND 106)	6
109	EMBASE	(101 AND 106)	27
110	EMBASE	exp "THROMBOSIS PROPHYLAXIS"/ OR exp "THROMBOSIS PREVENTION"/	9646
111	EMBASE	(64 AND 110)	5
112	EMBASE	(35 AND 110)	3
113	EMBASE	(56 AND 110)	7
114	EMBASE	(thromboprophylaxis).ti,ab	6014
115	EMBASE	(56 AND 114)	2
116	EMBASE	exp "SPONTANEOUS ABORTION"/	36500
117	EMBASE	(114 AND 116)	75
118	EMBASE	(64 AND 114)	4
119	EMBASE	exp "TIME FACTOR"/	13553
120	EMBASE	(42 AND 75 AND 119)	0
121	EMBASE	(40 AND 75 AND 119)	0
122	EMBASE	(duration).ti,ab	718593
123	EMBASE	(Hypercoagulability).ti,ab	5408

124	EMBASE	(75 AND 122 AND 123)	12
125	Medline	(Hypercoagulability ADJ3 pregnancy).ti,ab	45
126	Medline	exp "TIME FACTORS"/	1094868
127	Medline	(125 AND 126)	0
128	Medline	(Hypercoagulability ADJ3 maternal).ti,ab	11
129	Medline	(pregnan*).ti,ab	427589
130	Medline	(26 AND 126 AND 129)	54
131	Medline	(3 AND 126 AND 129)	47
132	Medline	(abortion ADJ2 haemostasis).ti,ab	0
133	Medline	(abortion ADJ2 hemostasis).ti,ab	4
134	Medline	exp HEMOSTASIS/	106250
135	Medline	(23 AND 134)	100
136	Medline	(defibrination).ti,ab	463
137	Medline	(8 AND 136)	0
139	Medline	134 AND 8	143
140	Medline	(23 AND 136)	11
141	Medline	(Hypercoagulability OR hypercoagulable OR hypercoagulation).ti,ab	7842
142	Medline	(8 AND 141)	71
143	Medline	(126 AND 129 AND 141)	18
144	EMBASE	(Hypercoagulability OR hypercoagulable OR	11846

		hypercoagulation).ti,ab	
145	EMBASE	(53 AND 144)	56
146	EMBASE	(prothrombo*).ti,ab	7860
147	EMBASE	(75 AND 119 AND 146)	0
148	EMBASE	(53 AND 146)	33
149	EMBASE	exp PUERPERIUM/	54560
150	EMBASE	(144 AND 149)	175
151	EMBASE	(146 AND 149)	79
152	EMBASE	*HEMOSTASIS/	29315
153	EMBASE	(35 AND 152)	11
154	EMBASE	(56 AND 153)	0
155	EMBASE	(56 AND 152)	13
156	EMBASE	(116 AND 152)	181
157	Medline	exp "POSTPARTUM PERIOD"/	56673
158	Medline	(141 AND 157)	40