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Pledge ceremony during observance of vigilance awareness week 2014

Scientific Advisory Committee Meeting of the institute

Participants and Faculty for Workshop on PID Flow Cytometry

Training Programme on Transfusion Medicine for North East region

Circulating cell-derived procoagulant microparticles in women with unexplained recurrent pregnancy loss

Rucha Patil

Summary:

Recurrent pregnancy loss (RPL) affects up to 15% of the reproducing couples and recurs in 2% to 3% of them. The diagnosis takes a toll on the couple, both emotionally and financially as despite a wide range of investigations, no apparent cause can be found in more than 50% of cases. A defective maternal hemostatic response leading to uteroplacental thrombosis along with hypoxia has been hypothesized to subsequently lead to adverse pregnancy outcomes like pregnancy loss, abruption placentae, intrauterine growth restriction/ death and preeclampsia. Thrombophilia, both genetic and antiphospholipid antibodies (APLA) have been described as risk factors for increasing susceptibility to adverse pregnancy outcome. However even after these investigations many cases remain unexplained. A new prothrombotic marker has surfaced which has been found associated with many thrombosis complicated conditions: the circulating cell-derived microparticles. Annexin V and endothelial MPs have been found to be increased in women with recurrent miscarriages. Hence, MPs appear as a valuable marker for the detection of in vivo cell activation and might have a pathogenic potential in RPL. If so, the next question that arises is whether antithrombotic therapy proves to be helpful in patients with elevated MPs.

Introduction

Pregnancy itself may be considered a hypercoagulable state wherein changes occur in the blood coagulation system in favor of the procoagulant branch with decreased levels of anticoagulant factors and increased levels of procoagulant factors. Pregnancy loss (PL) is the most common complication of pregnancy; the common causes include anatomical defects, chromosomal aberrations, endocrine factors, infections and other immunological factors. Recurrent pregnancy loss (RPL) is defined as two or more failed pregnancies, wherein the pregnancy is defined as a clinical pregnancy documented by ultrasonography or histopathological test [ASRM, 2013]. The diagnosis of RPL takes a toll on the couple, both emotionally and financially as despite a wide range of investigations, no apparent cause can be found in more than 50% of cases.

A defective maternal hemostatic response leading to uteroplacental thrombosis along with hypoxia has been hypothesized to subsequently lead to adverse pregnancy outcomes like PL, abruption placentae, intrauterine growth restriction/ death and preeclampsia. When a patient has a tendency to form blood clots, the condition is called thrombophilia. Thrombophilia can be an inherited disorder due to various predisposing genetic polymorphisms or mutations or it can be acquired due to APLA. Thrombophilia, both genetic and acquired have been described as risk factors for increasing susceptibility to adverse pregnancy outcome and anticoagulant treatment like aspirin, heparin, low or immunosuppressive doses of corticosteroids, etc. are proposed in cases with thrombophilia and have also proven to be beneficial.

Recently, a new prothrombotic marker has surfaced which has been found associated with many thrombosis complicated conditions: the circulating cell-derived microparticles. Elevated MPs have been found in several prothrombotic conditions like deep vein thrombosis (DVT), pulmonary embolism, stroke, acute coronary syndromes. Annexin V and endothelial MPs have been found to be increased in women with recurrent miscarriages (RM). Hence, MPs appear as a valuable

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marker for the detection of in vivo cell activation and might have a pathogenic potential in RPL. If they do have a role in RPL, the next question that arises is whether antithrombotic therapy proves to be helpful in patients with elevated MPs.

What are cell-derived Microparticles?

Microparticles (MPs) are submicronic vesicles derived from a variety of cell types and are found in both normal healthy condition and under different pathological conditions. They are phospholipid vesicles ranging in size from 0.1 to 1um, originating from different cell types including platelets, endothelial cells, leukocytes and red blood cells (RBC) besides several other cell types. They predominantly contain phospholipids and proteins, the latter being identification tag for the cells from which they originate (Figure 1). MPs may also contain deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). They are released from cell membranes during activation or apoptosis. As there is a continuous activation of different cells in our body, it is natural to expect MPs even under normal physiological conditions [Jy et al. 2010]. Due to their small size they easily escape the phagocytic system and remain for a longer time in the blood circulation as compared to the cells from which they originate.

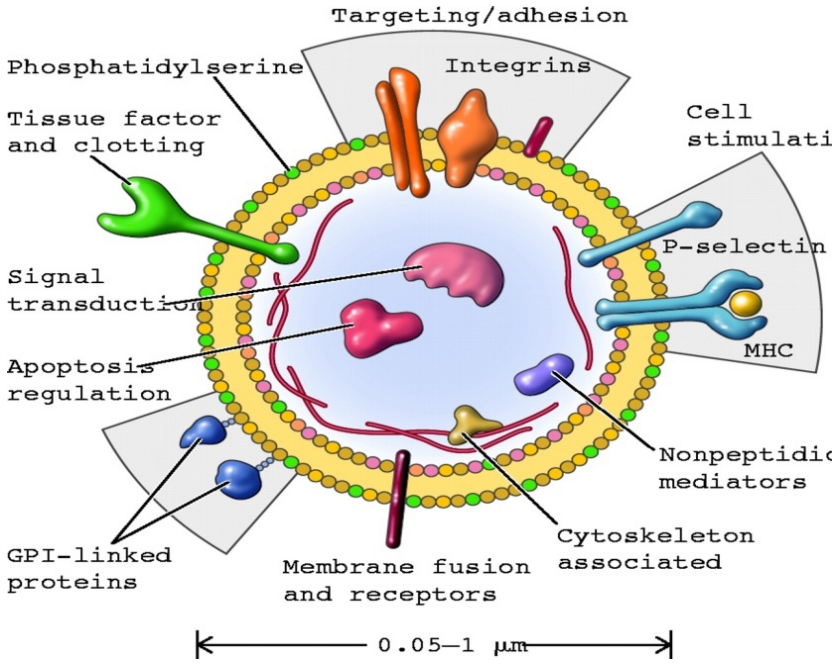

Figure 1: Structure of Microparticles [Adapted from Hugel B *et al*. 2005]

Properties

Various functions have been attributed to MPs by different authors. Being highly thrombogenic in nature, specifically platelet derived MPs, they have been associated with different thrombotic groups; myocardial infarct, DVT, pulmonary embolism and stroke. Besides being thrombogenic, MPs are also known to be pro inflammatory, proangiogenic and have been found to have a role in vascular dysfunction [Huisse et al. 2009, Mallat et al. 2000]. Some authors have also reported an immunomodulatory role for MPs [Jy et al. 2010, Zahra et al. 2011]. Increasingly, MPs have been reported to have a role in tumorigenesis. MPs shed from tumor cells reflect the metastatic potential of the tumor. Because of their minute size, they easily escape the phagocytic system and remain in circulation for longer period. The concentration of tumor derived MPs increases in blood with the progression of the disease, thus may serve as prognostic markers [Auwerda et al. 2011, Tilley et al. 2008].

Mechanism of MP formation

In resting cells, there is an asymmetrical distribution of phospholipids with phosphatidylcholine and sphingomyelin on the outer surface of cell membrane and phosphatidylserine (PS) and phosphatidylethanolamine on the inner surface. During cell activation or apoptosis, there is an "inside- out" flipping of the plasma membrane exposing the PS and phosphatidylethanolamine on the outer surface and vice versa [Fadeel et al. 2009]. This phenomenon is presumed to be universally applicable for all the cells. MPs are released from cell membranes during activation or apoptosis (Figure 2). Exposure of PS on the outer surface provides a favorable stimulus for the initiation of coagulation process resulting in prothrombinase complex which ultimately results in thrombin generation. Different factors have been reported to be responsible for the initiation of this "inside-out" signal of the plasma membrane. They include cytokines, enzymes like anionic phospholipid translocase, scramblase, floppase and complement [Larsen et al. 2008]. Besides phospholipases, signal transduction pathways have also been reported to play an important role in the formation of MPs [Cybulsky et al. 2005]. Another hypothesis is that during cell activation or apoptosis, there is an influx of extracellular calcium, which subsequently leads to proteolysis of the cytoskeletal components [Pasquet et al. 1996].The role of MPs in maintaining normal hemostasis is best exemplified by a genetic disorder i.e. Scotts syndrome, a rare genetic disorder, where there is a deficiency of PS and microvesiculation [Satta et al. 1997].

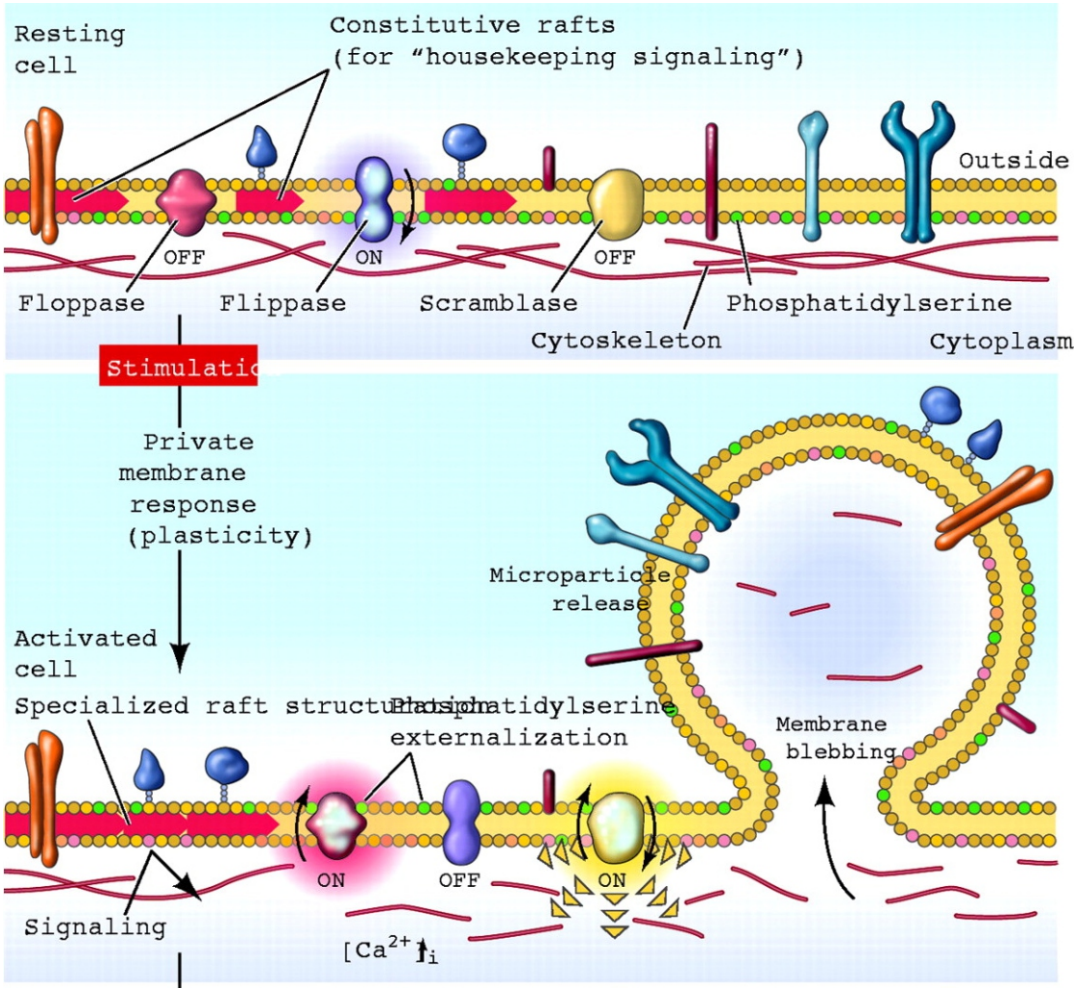

Figure 2: Formation of MPs [Adapted from Hugel *et al*. 2005]

Though platelet MPs are known to be highly thrombogenic, there are reports of TF bearing MPs released from monocytes and endothelial cells exhibiting high degree of thrombogenicity [Auwerda et al. 2011] TF is a known activator of blood coagulation which along with coagulation factor VII initiates the extrinsic pathway of coagulation. Another important mechanism by which MPs induce procoagulant atmosphere is by direct activation of other cells. Platelets are shown to get activated by MPs originating from neutrophils carrying surface markers CD11b/CD18 [Angelillo - Scherrer 2012].

An interesting study by Sugimura et al. (1999) has shown that injection of PS vesicles to pregnant mice increased thrombin generation in the placental bed resulting in intrauterine growth retardation (IUGR). Interestingly this was inhibited by simultaneous injection of annexin V.

Methods of detection

Methods for detection of these MPs are still evolving. MPs can be detected by:

- Microscopy- confocal and electron microscopy
- Enzyme linked immunoassays (ELISA)
- Clot based assays
- Flow cytometry.

Flow cytometry is the preferred method because of the ability to quantitate multiple antigens using multicolored fluorescent dyes. There are various pre-analytical and analytical variables in the isolation and quantitation of MPs. The International Society of Thrombosis and Haemostasis (ISTH) Scientific and Standardization subcommittees have already initiated their work on establishing certain criteria on pre-analytical and analytical variables affecting MP quantitation by flow cytometry [Lacroix et al. 2010]. Both confocal and electron microscopy have shown the presence of MPs. The commonly used ELISA technique for the detection of MPs is the capture of MPs onto annexin coated plates. The principle of functional assays or clot based assays is to measure the procoagulant activity of MPs either in an activated partial thromboplastin time (APTT) based or in a system using activated factor X. Different Abs specific to different cell sources are used in the analysis of MPs (Table 1).

Microparticles during healthy pregnancy

Overall, there is an increased risk of thrombosis during pregnancy due to ongoing cell activation throughout pregnancy and in postpartum period. This is evident by the presence of both acquired and hereditary thrombophilia in a large number of women undergoing miscarriages, preeclampsia (Pe), gestational hypertension, IUGR and others. Though there is an increase in the MP levels during normal pregnancy, in vitro experiments have shown them to be ineffective in causing endothelial dysfunction as against MPs isolated from women with Pe [Vanwijk et al. 2002].

Very few studies are available in literature on the levels of MPs of different cell types at different trimesters during normal pregnancy, In a study by Orozco et al. (2009) the number of total MPs were 9.3 × 106 MPs/ml , 18.3 × 106 MPs/ml and 23.0 × 106 MPs/ml respectively during first, second and third trimester. There was no significant difference in the levels of MPs between normal pregnancies in any of the trimesters and non-pregnant controls suggesting that these MPs are just an indication of normal apoptosis and not related to pregnancy. However fetal-derived human leukocyte antigen (HLA)-G or placental alkaline phosphatase DNA associated MPs were significantly higher in normal pregnant women as compared to non-pregnant controls. Increased prevalence of endothelial and platelet MPs in normal healthy pregnant women as against non-pregnant controls has been reported by several authors [Alijotas-Reig et al. 2012]. Even the procoagulant activity of the total annexin positive MPs was found to be increased in normal pregnancy as compared to no pregnant controls. Van Wijk et al. (2002) reported a decrease in suppressor T cell MPs (CD8+) during normal pregnancy as compared to healthy controls. This is expected as there is a generalized immune suppression throughout pregnancy. Lok et al. (2009) have reported that during pregnancy at 12 weeks, MPs were reduced in number which subsequently gets normalized to the post-partum levels.

Recurrent pregnancy loss and Thrombosis

When a patient has a tendency to form blood clots, the condition is called thrombophilia. It can be a life-threatening event if the clots restrict blood flow in critical organs like lungs, brain etc. Thrombophilia can be an inherited disorder due to various predisposing genetic polymorphisms or mutations or it can be acquired due to APLA. Other predisposing risk factors for thrombosis are external events such as surgery, obesity, pregnancy, dehydration (prolonged labour) and infection, use of oral contraceptives or long periods of immobility.

A hypothesis exists that many cases of RPL are caused by a defective maternal hemostatic response leading to thrombosis of the uteroplacental vasculature and subsequent fetal loss (Figure 3). Impairment of trophoblast invasion, villitis, and placental microthrombi is the main mechanisms supposedly involved in the pathogenesis of RM [Rai 2003, Greer 1999].

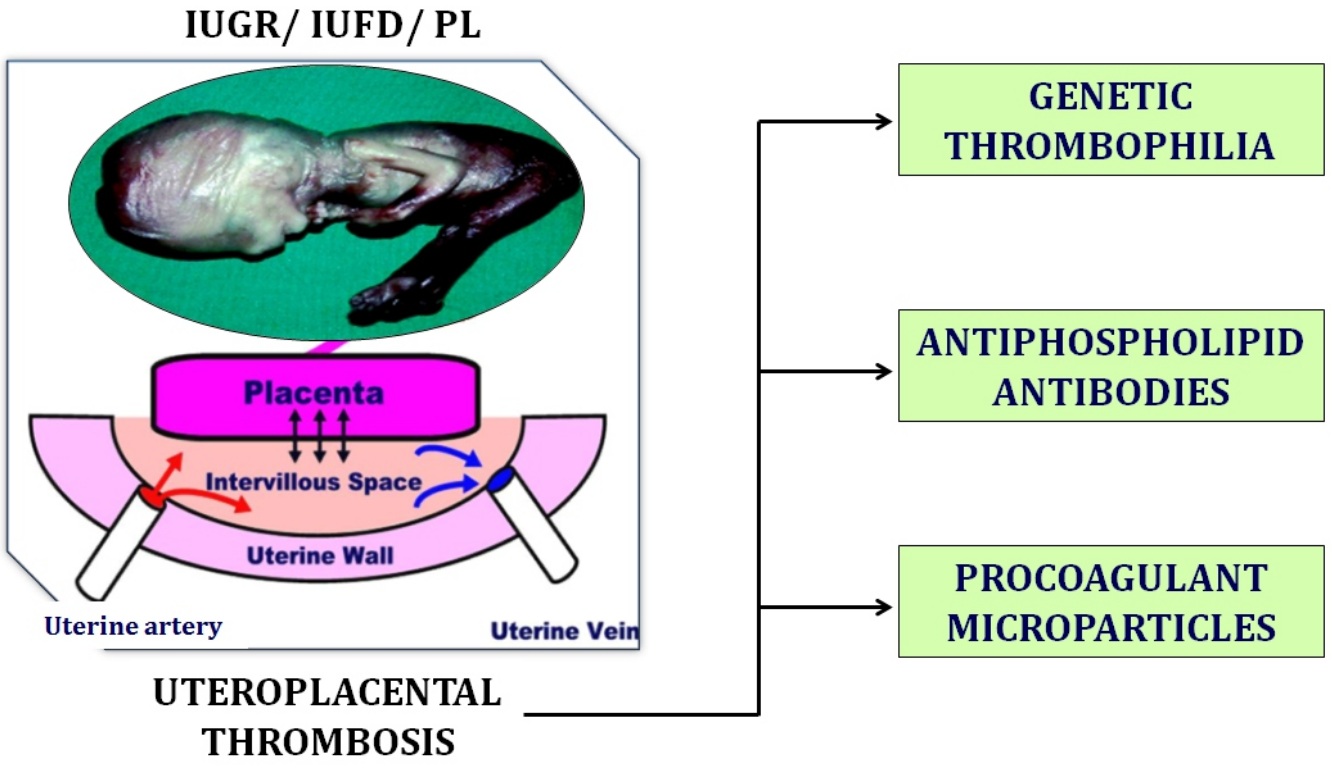

Figure 3: Uteroplacental thrombosis as a cause of recurrent pregnancy loss

Cell derived Microparticles as a cause of RPL

It has been hypothesized that annexin V is the main protein molecule which links MPs with adverse pregnancy outcome. Annexin V is an anticoagulant present in high concentrations on the outer surface of trophoblast membrane and is in direct contact with maternal blood. Rand et al. (1994) have also associated RM with APS through annexin V by reduction of the protein in the placental surface resulting in a prothrombotic condition. In the same line it has been assumed that since annexin V has a strong affinity for PS, it results in the accumulation of prothrombotic phospholipid vesicles resulting in a procoagulant situation.

As many cases of RPLs are not being explained by the common thrombophilia markers, MPs seem to be the most plausible candidates as causative factors for RPL or other adverse pregnancy conditions. Contradictory reports are

available in literature about the association of MPs with PL. Though elevated MPs have been reported in most of these reports [Laude et al. 2001, Ogasawara et al. 2000, Carp et al. 2004, Kaptan 2008, Alijotas-Reig et al. 2011, Pasquier et al. 2013] at least a few have reported decrease in MPs in RM cases as compared to controls [Toth et al. 2008]. Laude et al. (2001) studied 74 women with RM, 49 being early PL (before 10th GW) and 25 being late PL (beyond 10th GW) and showed the prevalence of MP prothrombotic activity much higher in both the groups as compared to nonpregnant healthy controls. The occurrence of higher levels of MPs in the early PL group is important in that majority of the women in this group have chromosomal anomalies rather than the vascular aberrations [Ogasawara et al. 2000]. Carp et al.(2004) studied 96 women with RM, and showed that endothelial MPs are increased in women with RM with an OR of 6.29. Kaptan et al.(2008) studied 20 women with RM and showed that platelet MP levels were significantly higher in women with RM while the platelet activation marker, P- selectin was found to be marginally increased. On the other hand, Alijotas-Reig et al. (2011) studied 30 women with RM, 16 with unexplained PL, and 7 with RM + unexplained PL and reported a significant decrease in endothelial MP in whole group of PL as also with RM group. Toth et al. (2008) studied 51 women with RM and did not find significant difference between cases and controls with regard to total number of MPs or endothelial MPs or platelet MPs. Pasquier et al. (2013) studied MPs in 124 women suffering from unexplained PLs and 273 parous women without PL. The study women displayed statistically significantly lower platelet and higher endothelial MP levels than the controls.

Association of MPs with acquired and genetic thrombophilia

There are many studies which have shown an association of MPs with other thrombophilia markers. Circulating platelet and leukocyte MPs have been found to be elevated in carriers of factor V leiden (FVL) mutation and may be important contributors to risk of thrombosis [Enjeti et al. 2010, Campello et al. 2012]. Higher levels of circulating MP were found in prothrombin G20210A mutation carriers and may play a role in the development of venous thrombo embolism (VTE) possibly by increasing thrombin generation [Campello et al. 2014]. Elevated plasma levels of endothelial MP were found in patients with APLA and in SLE patients with APLA but not in SLE patients without APLA and in non APLA related thrombosis. Endothelial MP levels were also associated with LA [Dignat-George et al. 2004]. Another study showed high number of endothelial MPs expressing TF in APS patients [Vikerfors et al. 2012].

Anticoagulant therapy (ACT) during pregnancy

Anticoagulation is essential in a wide variety of conditions in women of childbearing age. Some, such as VTE, occur more often during pregnancy. Others, such as RPL in the setting of APLA or other thrombophilia markers, are specific to pregnancy.

ACT is used during pregnancy for both prophylaxis and treatment of VTE. It is also employed for the prevention of intra uterine growth retardation (IUGR) and PL associated with the APLA and other thrombophilia markers. While anticoagulants are useful in many circumstances, their use during pregnancy increases the risk of hemorrhage and other adverse effects on the mother and the fetus. Treatment with anticoagulants during pregnancy must therefore be carefully considered, with judicious selection of the agent, and with reflection on the physiologic changes of pregnancy to ensure appropriate dosing. Several treatments have been proposed to prevent miscarriage some of which are aspirin, heparin, intravenous immunoglobulins (IVIG) and so on (Table 2). These act through either the coagulation cascade or the immune system.

NIIH Experiences:

ISTH Scientific and Standardization Subcommittees have initiated such a project which aims to standardize MP analysis on flow cytometer. NIIH is the only one centre from India and is a part of this project which included 40 laboratories worldwide accounting for 59 flow cytometers and by continuing to be a part of this project not only our flow cytometer has been validated for MP analysis but the technique is continuously being updated using the latest reagents like Megamix beads, Megamix SSC beads (Biocytex, Marseille, France).

At NIIH, procoagulant MPs- PS expressing MPs along with those of platelet, endothelial, leukocyte and erythrocyte origin as well as tissue factor expressing MPs was studied in 200 women suffering from unexplained RPL and was found to pose a high risk in such patients. This is the first study from India. The results were cross verified by using the STA- Procoag-PPL clotting time assay which measures procoagulant activity. 45%, 57.5% and 34.5% patients showed elevated annexinV, endothelial(CD62e) & TF(CD142) MPs, respectively (95% CI, $p<0.05$). Elevated MPs at a distance from pregnancy loss suggests a continued chronic endothelial damage/activation which may get exaggerated at the onset of pregnancy [Patil et al. 2013] (Figure 4). The next question which comes to mind is whether ACT which has proven to be beneficial in patients with other thrombophilia markers, prove to be beneficial in such patients with increase MPs. Thus the effect of anticoagulants- heparin, either low molecular weight (LMWH) or unfractionated (UFH), along with aspirin on MP levels and pregnancy outcome was studied in 25 pregnant women with PL history and on ACT and 25 healthy pregnant controls. Out of the 25 women on ACT, 20 patients had exaggerated MPs at the onset of pregnancy. In 15, MPs decreased as ACT continued & in 14, the levels normalized; the outcome being successful pregnancy with live births. In a search for the cause and diagnosis of unexplained PL, the results seem to be promising. We found that MPs decreased significantly as ACT progressed and successful pregnancy outcome was observed where MPs normalized. The data suggests that MPs may serve as important biomarkers for monitoring anticoagulation therapy and they may provide indications for adjustment of heparin/aspirin dosage or other therapeutic options so as to decrease and normalize the MP levels. This novel finding can be extended to other thrombosis complicated diseases where MPs have been found to be associated like deep vein thrombosis, myocardial infarction, etc.

From India, this is the first study on the role of procoagulant MPs in RPL. Worldwide, there is no data on the effect of anticoagulants like heparin on MPs.

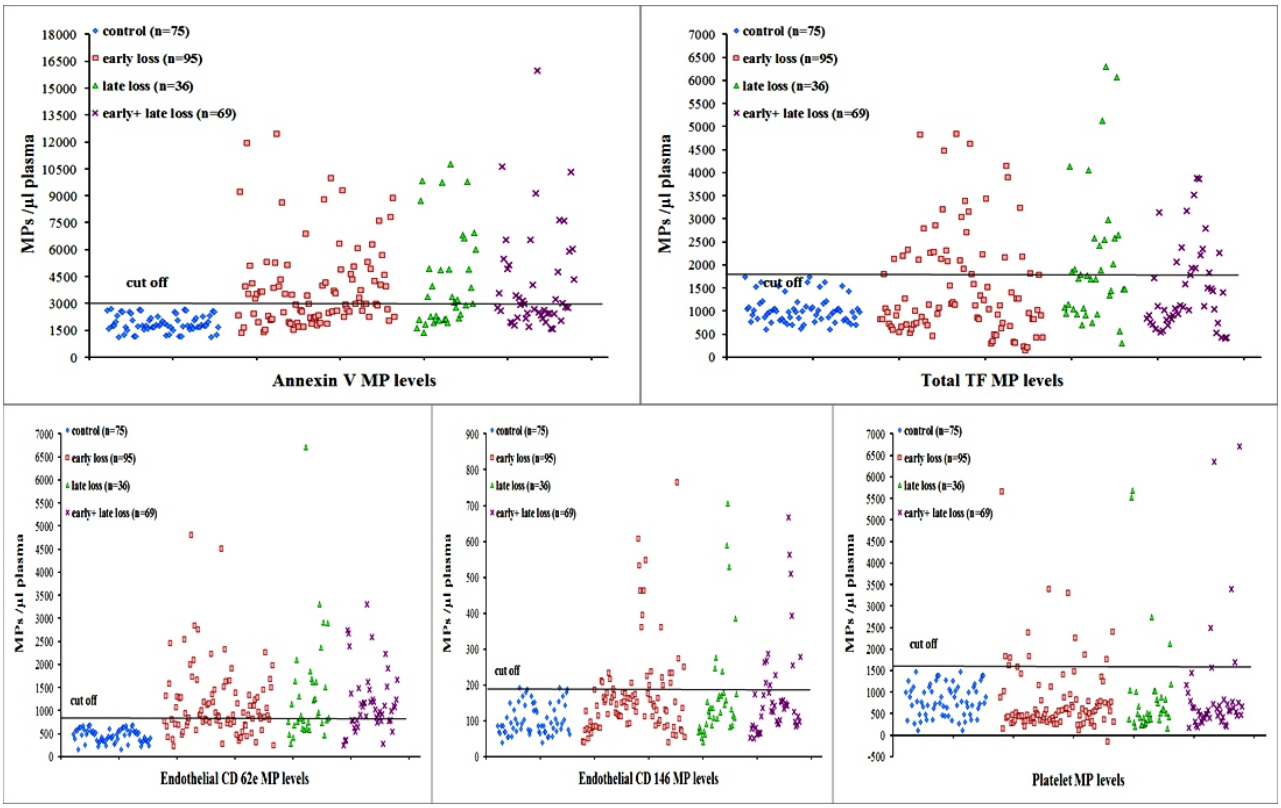

Figure 4: Scatter plot of MP levels in patients and controls

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Table 1: Different antibodies used for MP analysis from different cell sources

	Parent cell	**CD markers**	**Antigen**	**Expression**
1	Platelets	CD 41	Intact GP IIbIIIa	Constitutive
		CD 41a	GP IIbIIIa	Constitutive
		CD 42a	GP IX	Constitutive
		CD 42b	GP Ib	Constitutive
		CD 61	Integrin β3 chain GPIIIa	Constitutive
		CD 62P	P-selectin	Activated
2	Endothelial	CD 31^{+} CD $42b^{-}$	PECAM-1	Constitutive
	cell	CD 62E	E-Selectin	Activated
		CD 106	VCAM 1	Activated
		CD 105	Endoglin	Constitutive
		CD 144	VE Cadherin	Constitutive
		CD 51	Vitronectin receptor α	Constitutive
		CD 146	MUC-18/S-Endol	Constitutive
3	Leukocytes			
A	Leukocytes	CD 45	Leukocyte common Antigen (LCA)	Constitutive
B	Monocyte	CD 14	Lipopolysaccharide LPS receptor	Constitutive
C	Macrophage/	CD 11b	Integrin α M, Mac 1	Constitutive
	monocyte			
D	Granulocytes	CD 66b/ CD 66	CEACAM 8	Constitutive
E	Leukocytes	CD 11a	Lymphocyte function-associated antigen 1	Constitutive
F	T-helper	CD 4		Constitutive
	lymphocytes			
G	T- suppressor	CD 8		Constitutive
	lymphocytes			
H	Lymphocytes	CD 3		Constitutive
I	B-	CD 20	Activated-glycosylated phosphoprotein	Constitutive
	lymphocytes			
J	Granulocytes	CD 15	3-fucosyl-N-acetyl-lactosamine	Constitutive

Table 2: Different anticoagulant treatments given during pregnancy [Gibson PS *et al*, 2009]

MEDICATION	ACTION	INDICATIONS IN PREGNANCY	RECOMMENDED DOSAGE
Low molecular weight heparin (LMWH)	Potentiates antithrombin action, inactivates factor Xa much more than factor II (prothrombin)	To treat acute VTE Ongoing anticoagulation in women on long term anticoagulation To prevent VTE To prevent recurrent miscarriage (with aspirin) in APLA	**Therapeutic use** Enoxaparin 1mg/kg twice daily Dalteparin 100IU/kg twice daily Tinzaparin 175 IU/ kg twice daily **Prophylactic use** Enoxaparin 30 mg twice daily or 40 mg once daily Dalteparin 5000IU once daily Tinzaparin 75 IU/ kg once daily, or 4500 IU/ once daily
Unfractionated heparin (UFH)	Potentiates antithrombin action, inactivates factor Xa and factor II	To treat acute VTE Ongoing anticoagulation in women on long term anticoagulation To prevent VTE To prevent recurrent miscarriage (with aspirin) in APLA	**Therapeutic use** Intravenous: 80 U/kg bolus, then 18 U /kg/hour, adjusted to an APTT of 60 - 80 secs Subcutaneous: initial dose of 216 U/kg every 12 hours, adjusted to a mid-interval (6-hour) APTT of 60- 80 secs **Prophylatic use** 5000 U twice daily in 1st trimester 7500 U twice daily in 2nd trimester 10000 U twice daily in 3rd trimester
Warfarin (Coumadin), other coumarins	Reduce hepatic synthesis of factors II, VII, IX and X by inhibiting vit K	To prevent valve thrombosis and thromboembolism in women with a mechanical heart valve, gestational weeks 12 to 36 Postpartum anticoagulation for any indication	Initial dose 5-10 mg once daily, adjusted to an international normalized ratio of 2.0- 3.0
Aspirin	Inhibits platelet aggregation	To prevent recurrent miscarriages (with LMWH or UFH) in APLA To prevent Pe in high risk women	81 mg once daily

Dr K Ghosh, Director

1. Attended the National Task Force Meeting on Developing a Model for Thalassemia Control in Delhi and Chandigarh at ICMR Headquarters 22nd September 2014.
2. Attended the DGHS meeting on "Genetica Blood Disorder" at Nirman Bhavan, New Delhi on 15th October 2014.
3. Attended the Project Review Committee meeting by LSRB at Chennai on 19th October 2014.
4. Attended the 7th Annual ICS Meeting and Indo-US Clinical Cytometery Workshop 2014 and delivered the keynote address at AIIMS, New Delhi on 25th October 2014.

Department of Hemato-Genetics

Dr Roshan Colah, Scientist F

1. Visited Chandrapur along with the Director for planning the infrastructure to be developed to initiate work on hemoglobinopathies.
2. Invited to participate in the National Task Force Meeting on Developing a model for thalassemia control in Delhi and Chandigarh at ICMR Headquarters on 22nd September, 2014.
3. Awarded the "OPPI-Woman Scientist Award – 2014" by the Organization of Pharmaceutical Producers of India on 27th September, 2014.
4. Attended the mini Pre-Sac meeting at RMRC, Jabalpur on 29th September 2014.
5. Invited as a chairperson of the Technical Committee for Purchase of Equipment at EVRC (ICMR), Haffkine Institute on 13th October, 2014.
6. Organized a meeting of Investigators of 2 new multicentric projects on "Micromapping of G6PD deficiency" and "Establishment of Prenatal Diagnosis of Hemoglobinopathies" under the Tribal Health Research Forum on 17th October, 2015.
7. Invited to give a talk on "Strategies for Community Control of Hemoglobinopathies " at the Annual Conference of Indian Society of Hematology and Transfusion Medicine at Hyderabad on 6th November, 2014.
8. Conducted the technical evaluation and quality testing of solubility test kits and hemoglobin electrophoresis kits for NRHM for Maharashtra State Govt. Centres as a member of the Expert Committee at Mumbai on 18th and 24th November, 2014.
9. Invited as an Expert for the Technical Resource Group Meeting for Laboratory Services under District Early Intervention Centre (DEIC), Rashtriya Bal Swasthiya Karyakram (RBSK) under MOHWF to evolve a SOP manual for DEIC Labs at AIIMS, New Delhi on 28th November, 2014.
10. Attended the Red Cross Blood Transfusion Sub-Committee Meeting at Indian Red Cross Society, Mumbai on 9th December, 2014.

Dr Malay Mukherjee, Scientist D

1. Invited as a WHO Advisor to the Evidence Review Group meeting on Point of Care G6PD Testing to support safe use of Primaquine for the Treatment of Vivax Malaria held at Geneva, Switzerland from 8th to 9th October 2014 and delivered a talk on "Influence of individual G6PD genetic variants found in India on severity of hemolysis".
2. Organized a meeting of Investigators of new multicentric projects on "Micromapping of G6PD deficiency" and "Establishment of Prenatal Diagnosis of Hemoglobinopathies" under the Tribal Health Research Forum on 17th October, 2015

Dr P S Kedar, Technical Officer

1. Presented a paper entitled "Recessive congenital methaemoglobinaemia: Clinical and Molecular spectrum in India" in the 55th Annual conference of ISHBT (HEMATOCON-2014) held at Hyderabad from 6th to 8th November 2014.

Ms Rati Devendra, Technician

1. Attended a workshop entitled "Research methodology – Basic Biostatistic" held at KEM Hospital, Mumbai from 24th Julay to 9th October 2014.
2. Attended a workshop entitled "In-Silico tools for the genomics data analysis" held at National Institute of Research in Reproductive Health, Mumbai from 9th to 11th December 2014.

Ms Snehal Martin, JRF

1. Attended a workshop entitled "Research methodology – Basic Biostatistic" held at KEM Hospital, Mumbai from 24th Julay to 9th October 2014.

Department of Transfusion Medicine

Dr Ajit Gorakshakar, Scientist E

1. Attended 39th Annual Conference of Indian Society of Blood Transfusion and Immunohematology (TRANSCON2014) held at Patiala from 17th to 19th October 2014 and delivered a talk entitled "Potential and hazards of Gene Therapy."

Dr Swati Kulkarni, Scientist C

1. Attended post conference Immunohaematology workshop of 55th Annual conference of Indian Society of Haematology and Blood Transfusion held at Hyderabad on 9th November, 2014 and delivered a lecture entitled "Rh discrepancies and selection of blood units in RhD variants and chronic transfusions".
2. Attended 39th Annual conference of Indian Society of Blood Transfusion and Immunohaematology held at Patiala from 17th to 19th October 2014 and delivered lectures and also presented papers;

Lectures:

i. Molecular genotyping and its application to Transfusion Medicine.

ii. Rare blood group registry- need of the hour.

Oral Presentation:

i. Molecular genotyping of Indian blood group system.

ii. Molecular Blood group genotyping in patients with Thalassemia.

iii. Antigen negative red blood cell inventory of Indian blood donors.

3. Organized Advanced training programme for the Medical Officers and Technicians from North eastern states as part of translational research project from 24th to 28th Nov 2014, at NIIH, Mumbai.

Department of Transfusion Transmitted Diseases

Dr Aruna Shankarkumar

1. Organized a Scientist meet on 7th October 2014 to create a forum for researchers to meet and forge new collaborations, and to provide a state of the art overview of the latest findings from clinical research in the field of health science/ infectious diseases.
2. Invited as a resource person and delivered a lecture on "Troubleshooting on HIV testing" in the EQAS workshop at SRL BYL Nair hospital, Mumbai on 28th Nov 2014.
3. Attended National NACO meet on ' Strengthening of HIV labs - The journey of three decades' held at New Delhi from 4th to 5th December 2014 and presented a poster entitled "The retrospective study which summarizes the impact of accrediation towards successful headway of National Reference Laboratory (NRL) Mumbai".
4. Attended Hindi workshop at National Institute of Virology (NIV) Pune from 18th to 19th December 2014 and made a presentation on "Role of maintenance department".

Ms. Kruti Bhavik Dalal, Student

1. Awarded as Junior Research scholar (JRS) by Lady Tata Memorial Trust.

Department of Cytogenetics

Dr V Babu Rao, Scientist D

1. Nominated as a member of selection committee to select LDC at NIRRH, Mumbai on 28th September 2014.
2. Invited to deliver a talk on "Update on Indian Fanconi anemia Registry" at Pediatric Hematology Oncology Conference (PHOCON14) held at Chennai on 11th October 2014.
3. Invited as a chairman for the selection committee to select JRF at NIRRH, Mumbai on 22nd October 2014.

Department of Clinical & Experimental Immunology

Dr Vandana Pradhan, Scientist B

1. Attended International Conference on Autoimmunity and Transplantation (ICAT-2014) held at Goa from 12th to 15th October 2014 and presented a poster entitled "Association between the angiotensin-converting enzyme gene insertion/deletion polymorphism and susceptibility to systemic lupus erythematosus in the Indian population".
2. Attended National Conference of Indian Immunology Society (IMMUNOCON- 2014) held at Madurai from 12th to 14th December 2014 as an invited speaker and delivered a talk on 'Anti-Neutrophil is Cytoplasmic Antibodies (ANCA) in Systemic Vasculitides and other related disorders'.

Department of Haemostasis and Thrombosis

Ms. Patricia Pinto, Student

1. Awarded Best Paper Award for the paper entitled "A Comprehensive Analysis of Risk Factors for FVIII Inhibitor Development in Indian Haemophilia A Patients" at the 55th Annual Conference of the Indian Society of Haematology & Blood Transfusion held at Hyderabad from 6th to 8th November, 2014.

Ms. Rucha Patil, Student

1. Awarded Best Poster Award for the paper entitled "Microparticles as potential biomarkers for anticoagulant therapy in women with pregnancy loss" at the 55th Annual Conference of the Indian Society of Haematology & Blood Transfusion held at Hyderabad form 6th to 8th November, 2014.

Library

Vijay Padwal, ALIO

1. Attended "General Body Meeting and Election of the Executive committee members of the Federation of All India ICMR Employees (FAIIE)" at ICMR Headquarters, New Delhi on 2nd and 3rd Nov. 2014.

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Investigators Meeting on Micro mapping of G6PD deficiency project

Rashtriya Ektaa Divas Rally

Farewell to Mr Krishna Kawnkar, Technician

Pledge ceremony during observance of Swachh Bharat Abhiyan 2014

Hindi Pakwada week Celebration

Dr Roshan Colah, Scientist F receiving OPPI-Woman Scientist Award – 2014

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