NEWSLETTER OF THE INDIAN COLLEGE OF OBSTETRICIANS & GYNAECOLOGISTS

ISSUE February 2017 | Pages 16

ICOG CAMPUS

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Pregnancy at Risk - Prediction and Action

President's Address

Dr. Rishma Pai
President FOGSI

It gives me great pleasure to know that the first ICOG E-Newsletter is being released. In todays digital world, this is the best way to stay connected. For the ICOG, the academic wing of FOGSI, this is a great way to communicate the latest developments and updates in our field.

It is very important to be in touch with our members constantly and make sure they are informed about all ICOG activities.

I wish the Chairperson Dr. Mala Arora, Secretary Dr. S. Shantha Kumari and entire executive committee of ICOG all the best and I look forward to working in harmony with them throughout the year for the benefit of all Fogsians and for the betterment of the health of the women of our country.

Chairperson's Address

Esteemed Fellows & members of ICOG

Advancing Standards of Education & Health Care practices" is the theme of our news letter ICOG Campus.

The first volume of the *ICOG Campus* for this year is entitled " **Pregnancy at Risk-prediction and Action"**

Pre ecclampsia (PE) contributes significantly to both maternal and neonatal morbidity and mortality. Newer screening tools that include biochemical markers like sflt, sEng and PLGF levels appear promising screening tools, especially when combined with uterine artery Doppler flow indices. A comprehensive review article on these new markers is included in this issue. If we are able to screen women who will develop severe PE at an early stage, we can refer them to higher centres where life threatening complications like ecclampsia, HELLP syndrome, renal failure, pulmonary edema and prematurity can be managed competently.

The **journal scan** section includes an article on PLGF measurements at 12,22 and

Dr. Mala Arora
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32 weeks for prediction of PE. Post partum hypertension appears to be better controlled with antihypertensive drugs like clonidine and captopril, which are contraindicated in pregnancy. Two interesting articles on *gestational diabetes* are included. The first one is on combination therapy with glyburide and metformin in optimizing glycemic control. The second one looks at fetal adrenal gland volume, which seems to correlate with maternal HbA1c levels. Another interesting article observes that mothers with *anti Ro/SSA* have a lower incidence of heart block if they are on hydroxylchloroquine.

A simplified algorhythm for **clinical management of HBsAg positive** pregnant patient is included in this issue.

To tickle your grey cells a **Quiz section** is provided by Dr. Abha Rani Sinha, chairperson of the quiz committee. The correct answers should be mailed to icogoffice@gmail.com Participants sending correct answers will have their names displayed in the quiz section of the next issue of ICOG Campus.

It will be the endeavor of the editorial team to address relevant issues in each volume of ICOG Campus and provide the reader with the latest journal scan as well as a clinical visual quiz. Fellows wishing to contribute to the journal scan section are welcome to send truncated articles with reference at icogoffice@gmail.com

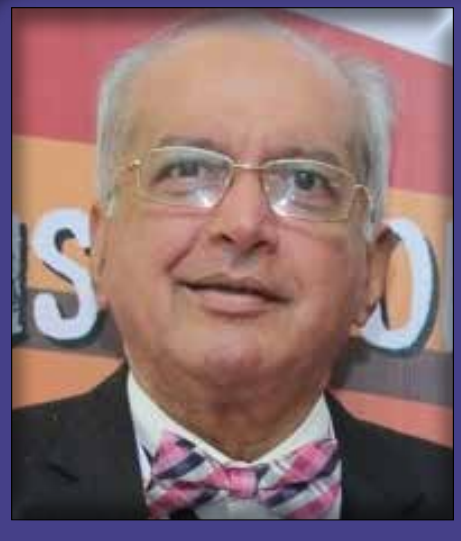
"What I learned from my work as a physician is that even with the most complicated patients, the most complicated problems, you've got to look hard to find every piece of data and evidence that you can to improve your decision-making. Medicine has taught me to be very much evidence-based and data-driven in making decisions."

- Jim Yong Kim

Message from Hon'ble Dean

Dear All!

It gives me immense pleasure to write this message for the inaugural issue of ICOG- Campus 2017. I extend my heartiest congratulations to Dr. Mala Arora and the editorial team led by Dr Monika Gupta for this wonderful and fruitful effort. I am confident that all the articles in this issue and all the forthcoming issues will be of utmost significance in the field of women healthcare. And, what better occasion than International women's day to launch the very first issue of this academic expedition.



Prof. C. N. Purandare
Dean ICOG

It is a matter of immense satisfaction for me to foresee that this medium of imparting knowledge will be a vital tool to accomplish the vision of our college, ICOG. I wish the whole team of ICOG-e-newsletter all the best.

Keep up the good work !

Secretary's Message

Warm greetings!

This is indeed a special moment. I am really happy and proud to share with you all that this all new revived endeavor of ICOG in the form of e-newsletter. Many congratulations to Dr Mala Arora for this well-conceived idea. I am sure, Dr Monika Gupta, the young talented enthusiastic academician, will do full justice as editor-in chief, to all the dedicated issues of this e-newsletter. In my view, the journal scan on special burning issues in obstetrics and gynaecology will be the highlight of every issue to apprise all readers with the latest evidence.

Dr. S. Shantha Kumari
Secretary ICOG

I wish all the success to the chair ICOG and the editorial team in their journey into the world of knowledge to bring forth many informative issues. I also urge all the ICOG members and fellows to reap the benefit from this effort into their day to day practices.

Happy reading to one and all…

Long live ICOG…

From the Editor's Pen

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Greetings and a warm welcome to all!

At the outset, I extend my heartfelt thanks to our dynamic ICOG Chairperson, Dr Mala Arora who has entrusted me to work in the capacity of editor-in-chief of this e-newsletter. Her vision to promote young talent through this great knowledge-sharing platform is undoubtedly commendable and me and my team will leave no stone unturned to live upto her expectations. It will be my continuous and dedicated effort to bring forth the best to achieve our goal of apprising everyone with the latest in field of obstetrics and gynaecology.

I am blessed to have a team of dynamic and vibrant members from academic background and varied fields of interests viz. Dr Bindiya Gupta, Dr Sharda Patra, Dr Reema Kumar, Dr Puneet Kochar. They will be complemented by Dr Abha Rani Sinha who will exclusively look after the intriguing Quiz section in all the issues.

We as a team will make a sincere effort to bring forth an academic bonanza every month. Our editions will largely be theme based with flavours of evidence based medicine. There will be an interesting review on a recent topic related to the theme supplemented by journal scan of recent most articles. A special highlight of every issue will be algorithm based checklist or guidelines regarding management of a challenging case scenario which will be a ready reckoner for practitioners.

This month's theme is **"Pregnancy at Risk- prediction and action"**. It includes a review article on newer markers for prediction of preeclampsia, an ever-challenging obstetric entity. There is an algorithm based management of a HbsAg positive woman complemented by an interesting journal scan of eight latest articles in field of high risk pregnancy. The brain teaser section will infuse enthusiasm into our inquisitive readers.

Your suggestions for the improvement of the newsletter and your contributions are highly valuable to us.

With this, on behalf of the Editorial team, I would like to wish happy reading to all of you.

COMING TOGETHER IS A BEGINING
KEEPING TOGETHER IS PROGRESS
WORKING TOGETHER IS SUCCESS
.....Henry Ford

I look forward to your feedbacks and encouragement.

ICOG Office Bearers – 2017

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Newer Markers in prediction of Preeclampsia: A review

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BACKGROUND

Preeclampsia affects 2-3% of all pregnancies and is a major cause of maternal and prenatal morbidity and death. It is mostly considered as a two-stage disorder. [1, 2]

- Stage 1 is pre clinical and occurs at the time of placentation. The endothelialization of cytotrophoblasts is impaired and the invasion of spiral arteries into myometrium is inadequate, remaining small caliber resistance vessels. Poor placentation results in possible placenta ischemia and hypoxia.
- Stage 2 occurs in late pregnancy. The oxidatively stressed placenta releases anti-angiogenic proteins such as soluble fms-like tyrosine kinase-1 (sflt-1), prostaglandins and cytokines into the maternal circulation.

Meanwhile, the hypoxic placenta reduces the production of pro-angiogenic factors including placental growth factor (PLGF) and vascular endothelial growth factor (VEGF). These changes cause the systemic endothelial dysfunction and an inflammatory response that leads to elevated systemic vascular resistance, vasoconstriction, activation of the coagulation cascade, and eventually clinical manifestations such as

- hypertension
- proteinuria
- hepatic dysfunction
- neurological disturbances
- hematological disturbances
- fetal growth restriction,
- rise in sflt-1
- downregulation of PLGF/VEGF

This imbalance results in abnormal placentation and placenta hypoxia that in turn results in imbalance of further angiogenesis, maternal endothelial dysfunction and preeclampsia. Thadhani et al. showed that the reduction of serum PLGF occurred as early as in the first trimester in patients destined to develop preeclampsia and suggested that imbalance of pro- and anti-angiogenic factors may be the primary cause of preeclampsia.[3]

Extensive research has been made in the last decade in screening for preeclampsia with the objective to

1. reduce the prevalence of the disease through pharmacologic intervention in the high-risk group[4]
2. minimize adverse perinatal events for those who experience preeclampsia by the determination of the appropriate time and place for delivery.[5]

The traditional approach to **screening** for preeclampsia is to identify risk factors from maternal demographic characteristics and medical history (maternal factors).[5] In pregnancies that experience preeclampsia, the mom values of uterine artery Pulsatility Index (PI) and mean arterial pressure (MAP) are increased, and the values of serum pregnancy associated placental protein A (PAPP-A) and PLGF are decreased. For all biomarkers, the deviation from normal is greater for early, rather than late, preeclampsia; therefore, the performance of screening is related inversely to the gestational age at which delivery becomes necessary for maternal and/or fetal indications.

Screening for preeclampsia by a combination of maternal factors,

- uterine artery PI,
- MAP, and
- serum PLGF at 11- 13 weeks gestation

can predict 75% of preterm-preeclampsia and 47% of term- preeclampsia, with a false positive rate of 10%. Such screening is superior to the respective values of 49% and 38% that are achieved by screening with maternal factors alone. The performance of screening by both biophysical and biochemical markers is superior to screening by either method alone. Here's a review of various preeclampsia-related pro- and anti-angiogenic factors (sflt-1, PLGF, and soluble Endoglin) and recent advances in the utilities of these markers for predicting Preeclampsia.

PLGF

PLGF is a member of the VEGF family that shares 42% amino acid sequence identity with VEGF, and they share significant structural similarity.[6] PLGF is a small protein (~30 kda) and is filtered into urine even in the absence of renal damage.[7] As the name suggested, PLGF was first identified in human Placenta.[8] It is expressed mainly in the villous cyto-trophoblasts and syncytio-trophoblasts which may indicate a role for placenta formation.[9] in normal pregnancy, the serum concentration of PLGF increases from 8-12 weeks, reaches to peak at 29-32 weeks, and then decreases at 33-40 weeks of gestation.[10] PLGF levels in women who later had preeclampsia were significantly lower than the controls. From 13-16 weeks of gestation till delivery and the PLGF was lowest in women with clinical preeclampsia at similar gestational age.[11] In a systematic review of 10 available studies, all reports consistently demonstrated a decrease of PLGF level in the second and the third trimester of pregnancy in patients with preeclampsia compared with normal pregnancy. The decrease of PLGF was shown to correlate with the severity of the disease in all those studies that investigated severe form of preeclampsia.[12] The ROC area under curve of PLGF for prediction of preeclampsia with onset prior to 34 weeks' gestation using serum specimens obtained 22-26 weeks' gestation was 0.97.[13] Because the change of PLGF happens earlier than that of sflt-1, it may be considered as a better marker for predicting Preeclampsia. Serum sflt-1 to PLGF ratio is significantly Increased in preeclamptic pregnancy compared with the control and it has shown a fairly good power for the prediction, with an area under the ROC curve as 0.94.[13,14] Another important aspect of PLGF is its small molecular size and easy filtration in urine, hence **urinary PLGF** may be used as a convenient preeclampsia marker. In the Calcium for Preeclampsia Prevention (CPEP) trial, Levine et al. found that during normal pregnancy urinary PLGF demonstrated the same pattern as serum PLGF, which increased during the first 2 trimesters, peaked at 29-32 weeks then decreased thereafter.[6] Similarly, urinary PLGF (from both random and first morning urine) increased in preeclamptic pregnancies but was significantly lower compared to controls.

SFLT-1

Also known as soluble fms like tyrosine kinase 1. The production of sflt- 1 is mostly from the placenta, with only small amounts that are generated by endothelial cells and monocytes.[15,16] Sflt-1 may play an important role in the pathogenesis of preeclampsia and may actually be the cause of the syndrome. In normal pregnancy, the serum concentration of sflt-1 decreases from 8-12 weeks to 16-20 weeks, gradually increases at 26-30 weeks, rapidly elevates at 35-39 weeks of gestation, and it is back to normal level after delivery.[11] However, sflt-1 level in preeclamptic pregnancy is significantly higher than that of normal pregnancy. Levine et al. have shown that the rise in sflt-1 levels began approximately five weeks before the onset of preeclampsia.[10,11] The mean serum concentration of sflt-1 in the women with the onset of clinical disease was highest and about 3 times of that of normal pregnancies of similar gestational age and its levels correlated with the severity of the

disease.[11,17] In a systematic review, all five available studies consistently demonstrated the increase of sflt-1 level after gestational week 25 in preeclampsia, especially in severe preeclampsia, compared with the control group.[12] The ROC curves of sflt-1 for prediction of preeclampsia, with onset prior to 34 weeks' gestation, was constructed using serum specimens obtained at 22-26 weeks' gestation and the area under curve was 0.9.[13] Hence sflt-1 has demonstrated diagnostic utilities to differentiate preeclampsia from normal pregnancy, gestational hypertension and chronic hypertension with sensitivities of 79-90%,specificities of 88-95%, positive likelihood ratio (LR) of 6.7-16, negative LR of 0.1-0.2, and area under the curve of 0.88-0.94.[18]

SOLUBLE ENDOGLIN

Endoglin, also known as CD105, is a trans-membrane glycoprotein first identified by Letarte's group.[19,20] Endoglin is highly expressed on the cell membranes of syncytiotrophoblasts, vascular endothelial cells, and it is also expressed on other cells such as monocytes and hematopoietic stem cells.[21] Soluble Endoglin (sEng) is the 65 kda truncated form of Endoglin.[22] Evidence indicated that sEng is an anti angiogenesis factor and it contributes to the pathogenesis of preeclampsia.[48] It has been shown to impair the binding of TGF-1 to its receptors and downstream signalling such as activation of endothelial nitric oxide synthase (e nos) and vasodilation.[23] Adenoviral mediated over expression of sEng in pregnant rats led to hypertension, and co-administration of sEng and sflt-1 resulted in severe preeclampsia including the HELLP syndrome.[24] In addition, sEng correlates tightly with sflt-1, PLGF, and ratio of sflt-1/PLGF, as well as disease severity in preeclampsia.[25] The serum level of sEng in normal pregnancy is quite stable till its slight increase at 33-42 weeks of gestation.[11] However, circulating sEng concentrations are significantly elevated in preeclamptic pregnancy and intrauterine growth restriction.[11, 26] Very interestingly, sEng levels increased significantly before the onset of disease in women with preterm preeclampsia (< 37 weeks) by 9-11 weeks, and in term preeclampsia (at > 37 weeks) by 12-14 weeks respectively.[11] The second trimester sEng levels have been suggested as a marker for predicting preterm and severe preeclampsia.[27,28] Soluble Endoglin has also demonstrated fairly good diagnostic utilities to differentiate preeclampsia from normal pregnancy, gestational hypertension and chronic hypertension with sensitivities of 84-90%, specificities of 79- 95%, positive LR of 4-17.9, negative LR of 0.1-0.2, and area under the ROC curve of 0.75-0.93.[18] The predictive abilities of sflt-1 and PLGF for preeclampsia were excellently reviewed by Widmer et al. In a systematic review[12] The test utility for sEng has been proven by some studies.[18, 14, 29, 30]

The ratio of sflt-1 to PLGF is elevated in pregnant women before the clinical onset of preeclampsia, but its predictive value in women with suspected preeclampsia is unclear. A prospective, multicenter, observational study to derive and validate a ratio of serum sflt-1 to PLGF that would be predictive of the absence or presence of preeclampsia in the short term in women with singleton pregnancies in whom preeclampsia was suspected (24 weeks 0 days to 36 weeks 6 days of gestation) was carried out. Primary objectives were to assess whether low sflt-1:PLGF ratios (at or below a derived cutoff) predict the absence of preeclampsia within 1 week after the first visit and whether high ratios (above the cutoff) predict the presence of preeclampsia within 4 weeks. The results of the study indicated that sflt-1:PLGFratio of 38 or lower can be used to predict the short-term absence of preeclampsia in women in whom the syndrome is suspected clinically.[31]

CONCLUSION

Circulating sflt-1, PLGF and sEng have specific alterations in preeclampsia pregnancies and because these changes usually happen before the onset of clinical presentation of the disorder, these proteins are believed to be useful for predicting preeclampsia. These angiogenic factors may be used as markers for the third or second trimester screening test, but before we adopt these strategies, there are several challenges to overcome. There is large variation in the published values of these markers within the same gestational age window which may reflect the heterogeneity in sample handling, processing and laboratory procedures, and this variation induces difficulties to compare the diagnostic values across different studies. In addition, there is no adequate information on a cut-off for clinical practice to predict preeclampsia. So far numerous studies provided the associations between alterations of angiogenic factors and subsequent preeclampsia, however most were retrospective studies with limited patients numbers. The evidence is insufficient to recommend these factors to be used for screening tests at present.[12] Prospective data with rigorous study design and enough patient participants are needed to further evaluate the clinical utility of these tests.

In conclusion, sflt-1,PLGF, and sEng are important angiogenic (both pro and anti) factors involved in the pathogenesis of Preeclampsia. These proteins may be promising markers for the disease prediction. With the early detection of preeclampsia, appropriate treatment, timely delivery and continued intensive postpartum monitoring, most cases of severe preeclampsia and eclampsia can be prevented. Although there is no curative treatment yet, these angiogenic factors may provide a potential for targeted therapy in the future.

REFERENCES

1. World Health Organization, Make every mother and child count. Geneva: World Health Report; 2005.
2. Borzychowski, A.M.; Sargent, I.L.; Redman, C.W. Inflammation and pre-eclampsia. *Semin. Fetal. Neonatal Med*., **2006**, *11*(5), 309-316.
3. Thadhani, R.; Mutter, W.P.; Wolf, M.; Levine, R.J.; Taylor, R.N.; Sukhatme, V.P.; Ecker, J.; Karumanchi, S.A. First trimester placental growth factor and soluble fms-like tyrosine kinase 1 and risk for preeclampsia. *J. Clin. Endocrinol. Metab*.,**2004**, *89*(2), 770-775.
4. Roberge S, Villa P, Nicolaides KH, et al. Early administration of low dose aspirin for the prevention of preterm and term pre-eclampsia: a systematic review and meta-analysis. Fetal DiagnTher 2012;31:141-6.
5. Koopmans CM, Bijlenga D, Groen H, et al. Induction of labour versus expectant monitoring for gestational hypertension or mild pre- eclampsia after 36 weeks gestation (HYPITAT): a multicentre, open-label randomized controlled trial. Lancet 2009;374:979-88.
6. Wright D, Syngelaki A, Akolekar R, Poon LC, Nicolaides KH. Competing risks model in screening for preeclampsia by maternal characteristics and medical history. Am J Obstet Gynecol 2015;213:62. e1-10.
7. Levine, R.J.; Thadhani, R.; Qian, C.; Lam, C.; Lim, K.H.; Yu, K.F.; Blink, A.L.; Sachs, B.P.; Epstein, F.H.; Sibai, B.M.; Sukhatme, V.P.; Karumanchi, S.A. Urinary placental growth factor and risk of preeclampsia. *JAMA*, **2005**, *293*(1), 77-85
8. Maglione, D.; Guerriero, V.; Viglietto, G.; Delli-Bovi, P.; Persico, M.G. Isolation of a human placenta cDNA coding for a protein re- lated to the vascular permeability factor. *Proc. Natl. Acad. Sci. USA*, **1991**, *88*(20), 9267-9271.
9. Torry, D.S.; Mukherjea, D.; Arroyo, J.; Torry, R.J. Expression and function of placenta growth factor: implications for abnormal pla- centation. *J. Soc. Gynecol. Investig*.,**2003**, *10*(4), 178-188.
10. Hirashima, C.; Ohkuchi, A.; Arai, F.; Takahashi, K.; Suzuki, H.; Watanabe, T.; Kario, K.; Matsubara, S.; Suzuki, M. Establishing reference values for both total soluble Fms-like tyrosine kinase 1 and free placental growth factor in pregnant women. *Hypertens. Res*., **2005**, *28*(9), 727-732
11. Levine, R.J.; Maynard, S.E.; Qian, C.; Lim, K.H.; England, L.J.; Yu, K.F.; Schisterman, E.F.; Thadhani, R.; Sachs, B.P.; Epstein, F.H.; Sibai, B.M.; Sukhatme, V.P.; Karumanchi, S.A. Circulating angiogenic factors and the risk of preeclampsia. *N. Engl. J. Med*., **2004**, *350*(7), 672-683.
12. Widmer, M.; Villar, J.; Benigni, A.; Conde-Agudelo, A.; Karuman- chi, S.A.; Lindheimer, M. Mapping the theories of preeclampsia and the role of angiogenic factors: a systematic review. *Obstet. Gynecol*.,**2007**, *109*(1), 168-180.
13. Moore Simas, T.A.; Crawford, S.L.; Solitro, M.J.; Frost, S.C.; Meyer, B.A.; Maynard, S.E. Angiogenic factors for the prediction of preeclampsia in high-risk women. *Am. J. Obstet. Gynecol*., **2007**, *197*(3), 244.el-8.
14. Levine, R.J.; Lam, C.; Qian, C.; Yu, K.F.; Maynard, S.E.; Sachs, B.P.; Sibai, B.M.; Epstein, F.H.; Romero, R.; Thadhani, R.; Karu- manchi, S.A.; CPEP Study. Soluble endoglin and other circulating antiangiogenic factors in preeclampsia. *N. Engl. J. Med*., **2006**, *355*(10), 992-1005.
15. Zhou, Y.; McMaster, M.; Woo, K.; Janatpour, M.; Perry, J.; Kar- panen ,T.; Alitalo, K.; Damsky, C.; Fisher, S.J. Vascular endothe- lial growth factor ligands and receptors that regulate human cytot-rophoblast survival are dysregulated in severe preeclampsia and hemolysis, elevated liver enzymes, and low platelets syndrome. *Am. J. Pathol*.,**2002**, *160*(4), 1405-1423.
16. He, Y.; Smith, S.K.; Day, K.A.; Clark, D.E.; Licence, D.R.; Char- nock-Jones, D.S. Alternative splicing of vascular endothelial growth factor (VEGF)-R1 (FLT-1) pre-mRNA is important for the regulation of VEGF activity. *Mol. Endocrinol*.,**1999**, *13*(4), 537- 545.
17. Chaiworapongsa, T.; Romero, R.; Espinoza, J.; Bujold, E.; Mee Kim, Y.; Gonçalves, L.F.; Gomez, R.; Edwin, S. Evidence support- ing a role for blockade of the vascular endothelial growth factor system in the pathophysiology of preeclampsia. *Am. J. Obstet. Gynecol*.,**2004**, *190*(6), 1541-1547.

18. Salahuddin, S.; Lee, Y.; Vadnais, M.; Sachs, B.P.; Karumanchi, S.A.; Lim, K.H. Diagnostic utility of soluble fms-like tyrosine kinase 1 and soluble endoglin in hypertensive diseases of preg- nancy. *Am. J. Obstet. Gynecol.*, **2007**, *197*(1), 28.e1-6
19. Quackenbush, E.J.;Letarte, M. Identification of several cell surface proteins of non-T, non-B acute lymphoblastic leukemia by using monoclonal antibodies. *J. Immunol.*,**1985**, *134*(2), 1276-1285.
20. Gougos, A.; Letarte, M. Primary structure of endoglin, an RGD- containing glycoprotein of human endothelial cells. *J. Biol. Chem.*, **1990**, *265*(15), 8361-8364.
21. Chen, C.Z.; Li, M.; de Graaf, D.; Monti, S.; Göttgens, B.; Sanchez, M.J.; Lander, E.S.; Golub, T.R.; Green, A.R.; Lodish, H.F. Identi fication of endoglin as a functional marker that defines long-term repopulating hematopoietic stem cells. *Proc. Natl. Acad. Sci. USA*, **2002**, *99*(24), 15468-15473.
22. Raab, U.; Velasco, B.; Lastres, P.; Letamendía, A.; Calés, C.; Langa, C.; Tapia, E.; López-Bote, J.P.; Páez, E.; Bernabéu, C. Ex- pression of normal and truncated forms of human endoglin. *Bio- chem. J.*, **1999**, *339*(Pt 3), 579-588.
23. Luft, F.C. Soluble endoglin (sEng) joins the soluble fms-like tyro- sine kinase (sFlt) receptor as a pre-eclampsia molecule. *Nephrol. Dial. Transplant.*,**2006**, *21*(11), 3052-3054.
24. Katesha, S.; Toporsian, M.; Lam, C.; Hanai, J.; Mammoto, T.; Kim, Y.M.; Bdolah, Y.; Lim, K.H.; Yuan, H.T.; Libermann, T.A.; Stillman, I.E.; Roberts, D.; D'Amore, P.A.; Epstein, F.H.; Sellke, F.W.; Romero, R.; Sukhatme, V.P.; Letarte, M.; Karumanchi, S.A. Soluble endoglin contributes to the pathogenesis of preeclampsia. *Nat. Med.*, **2006**, *12*(6), 642-649.
25. Masuyama, H.; Nakatsukasa, H.; Takamoto, N.; Hiramatsu, Y. Correlation between soluble endoglin, vascular endothelial growth factor receptor-1, and adipocytokines in preeclampsia. *J. Clin. En- docrinol. Metab.*,**2007**, *92*(7), 2672-2679.
26. Stepan, H.; Krämer, T.; Faber, R. Maternal plasma concentrations of soluble endoglin in pregnancies with intrauterine growth restric- tion. *J. Clin. Endocrinol. Metab.*,**2007**, *92*(7), 2831-2834.
27. Rana, S.; Karumanchi, S.A.; Levine, R.J.; Venkatesha, S.; Rauh- Hain, J.A.; Tamez, H.; Thadhani, R. Sequential changes in antian- giogenic factors in early pregnancy and risk of developing preeclampsia. *Hypertension*, **2007**, *50*(1), 137-142.
28. Robinson, C.J.; Johnson, D.D. Soluble endoglin as a second- trimester marker for preeclampsia. *Am. J. Obstet. Gynecol.*, **2007**, *197*(2), 174.e1-5.
29. Baumann, M.U.; Bersinger, N.A.; Mohaupt, M.G.; Raio, L.; Ger- ber, S.; Surbek, D.V. First-trimester serum levels of soluble en- doglin and soluble fms-like tyrosine kinase-1 as first-trimester markers for late-onset preeclampsia. *Am. J. Obstet. Gynecol.*, **2008**, 199(3), 266.e1-6.
30. Stepan, H.; Geipel, A.; Schwarz, F.; Krämer, T.; Wessel, N.; Faber, R. Circulatory soluble endoglin and its predictive value for preeclampsia in second-trimester pregnancies with abnormal uter- ine perfusion. *Am. J. Obstet. Gynecol.*, **2008**, 198(2), 175.e1-6.
31. 31 HaraldZeisler, M.D., Elisa Llurba, M.D., Ph.D., Frederic Chantraine, M.D., Ph.D., Manu Vatish, M.B., Ch.B., D.Phil., Anne Cathrine Staff, M.D., Ph.D., Maria Sennström, M.D., Ph.D., Matts Olovsson, M.D., Ph.D., Shaun P. Brennecke, M.B., B.S., D.Phil., HolgerStepan, M.D., Deirdre Allegranza, B.A., Peter Dilba, M.Sc., Maria Schoedl, Ph.D., Martin Hund, Ph.D., and Stefan Verlohren, M.D., Ph.D. Predictive Value of the sFlt-1:PlGF Ratio in Women with Suspected PreeclampsiaN Engl J Med 2016; 374:13-22 January 7, 2016 DOI: 10.1056/NEJMoa1414838

"The glory of medicine is that it is constantly moving forward, that there is always more to learn. The ills of today do not cloud the horizon of tomorrow, but act as a spur to greater effort".

- William James Mayo

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1. Glyburide Versus Metformin and Their Combination for the Treatment of Gestational Diabetes Mellitus: A Randomized Controlled Study.

Nachum Z, Zafran N, Salim R, Hissin N, Hasanein J, Letova YG, Suleiman A, Yefet E

Diabetes Care 2017 Jan 11.pii: dc162307.

Objective: To compare the efficacy and safety of glyburide versus metformin and their combination for the treatment of gestational diabetes mellitus (GDM).

Research Design and Methods: In this prospective randomized controlled study, we randomly assigned patients with GDM at 13-33 weeks gestation and whose blood glucose was poorly controlled by diet to receive either glyburide or metformin. If optimal glycemic control was not achieved, the other drug was added. If adverse effects occurred, the drug was replaced. If both failed, insulin was given. The primary outcomes were the rate of treatment failure and glycemic control after the first-line medication according to mean daily glucose charts.

Results: Glyburide was started in 53 patients and metformin in 51. In the glyburide group, the drug failed in 18 (34%) patients due to adverse effects (hypoglycemia) in 6 (11%) and lack of glycemic control in 12 (23%). In the metformin group, the drug failed in 15 (29%) patients, due to adverse effects (gastrointestinal) in 1 (2%) and lack of glycemic control in 14 (28%). Treatment success after second-line therapy was higher in the metformin group than in the glyburide group (13 of 15 [87%] vs. 9 of 18 [50%], respectively; P = 0.03). In the glyburide group, nine (17%) patients were eventually treated with insulin compared with two (4%) in the metformin group (P = 0.03). The combination of the drugs reduced the need for insulin from 33 (32%) to 11 (11%) patients (P = 0.0002). Mean daily blood glucose and other obstetrical and neonatal outcomes were comparable between groups, including macrosomia, neonatal hypoglycemia, and electrolyte imbalance.

Conclusions: Glyburide and metformin are comparable oral treatments for GDM regarding glucose control and adverse effects. Their combination demonstrates a high efficacy rate with a significantly reduced need for insulin, with a possible advantage for metformin over glyburide as first-line therapy.

2. Pro-Inflammatory Cytokine Levels in HIV Infected and Uninfected Pregnant Women with and without Preeclampsia.

Maharaj NR, Phulukdaree A, Nagiah S, Ramkaran P, Tiloke C, Chuturgoon AA

PLoS One. 2017 Jan 17;12(1):e0170063.

Introduction: Preeclampsia and HIV/AIDS are inflammatory conditions that contribute significantly to adverse maternal and fetal outcomes. The immune reconstitution effects of HAART on inflammatory mediators has not been adequately studied in pregnancy and may impact on the inflammatory cytokine network in women with co-morbid preeclampsia. Our study evaluated changes in pro-inflammatory cytokines IL-2, TNF-α, IFN-γ and IL-6 in HIV infected preeclamptic women on HAART.

Methods: A prospective experimental study was conducted at Prince Mshiyeni Memorial Hospital between July 2013 and September 2014. One hundred and ninety three pregnant women were recruited into 4 groups: uninfected normotensive (50; 26%), infected normotensive (45; 23%), uninfected preeclamptic (53; 28%) and infected preeclamptic women (45; 23%). Serum

levels of cytokines TNF-α, IFN- γ, IL-2 and IL-6 were determined using commercially available kits and a Cytometric Bead Array (CBA). Comparative data was recorded and analysed descriptively.

Results: In the control groups (normotensive), significantly lower values were found in IL-2 (p = 0.010), TNF-α (p = 0.045), and IL-6 (p = 0.005); and a non-significant decrease was observed in IFN-γ (p = 0.345) in HIV infected women on HAART compared to uninfected controls. In the experimental group (preeclamptic) women, significantly reduced levels were observed in IL-2 and TNF-α (p = 0.001; p = 0.000) and non-significant decreases were observed in IFN-γ and IL-6 (p = 0.023; p = 0.086) in HIV infected women on HAART compared with uninfected preeclamptic women. Non-significant differences were observed between uninfected preeclamptic and normotensive women.

Conclusion: In uncomplicated/normotensive pregnancies, HIV/HAART is associated with significant decreases in IL-2, TNF-α and IL-6, and in preeclamptic women significant decreases in IL-2 and TNF-α were observed. These findings suggest that HIV/HAART impacts on pro-inflammatory cytokines in women with co-morbid preeclampsia. This provides a platform for further research on immune reconstitution effects of HAART during pregnancy, and the development of potential immune modulation therapies for the management of preeclampsia.

3. **Repeat measurements of uterine artery pulsatility index, mean arterial pressure and serum placental growth factor at 12, 22 and 32 weeks in the prediction of preeclampsia.**

   Andrietti S, Carlucci S, Wright A, Wright D, Nicolaides KH

   Ultrasound Obstet Gynecol. 2017 Jan 12. doi: 10.1002/uog.17403. [Epub ahead of print]

Objective: To investigate the potential value of repeat measurements of uterine artery pulsatility index (UTPI), mean arterial pressure (MAP) and serum placental growth factor (PLGF) at 12, 22 and 32 weeks' gestation in the prediction of preeclampsia (PE) after 32 weeks.

Methods: The data were derived from prospective screening for adverse obstetric outcomes in women attending for their routine hospital visit at 11-13, 19-24 and / or 30-34 weeks' gestation in two maternity hospitals in England. UTPI, MAP and PLGF were measured. Bayes theorem was used to combine the a priori risk from maternal factors with UTPI, MAP and PLGF multiple of the median (MoM) values. The performance of screening for PE developing after the 30-34 weeks visit by UTPI, MAP and PLGF measured at 11-13, 19-24, 30-34 and their combinations was examined.

Results: Screening at 30-34 weeks by UTPI, MAP and PLGF detected, at 10% false positive rate, 79%, 86% and 92% of preterm-PE and 42%, 50% and 56% of term-PE. The addition of biomarker values obtained at 11-13 and / or 19-24 weeks was not associated with any improvement in the detection rate of preterm-PE; in the case of term-PE, there was a marginal (<2%) improvement in detection for UTPI and MAP and a modest improvement of about 5% for PLGF.

Conclusions: Measurements of UTPI, MAP and PLGF in the first- and / or second-trimester has a small or no effect in improving the prediction of PE provided by screening in the early third-trimester.

4. **Sonographic Evaluation of Fetal Adrenal Gland in Gestational Diabetes: Relation to Fetal Growth and Maternal Biochemical Markers.**

   Garcia-Flores J, Cruceyra M, Cañamares M, Garicano A, Espada M, Nieto O, Tamarit I, Sainz de la Cuesta R.J

   Ultrasound Med. 2017 Feb 2. doi: 10.7863/ultra.16.03005. [Epub ahead of print]

Objectives: To relate measurements and volume of the fetal adrenal gland in third trimester ultrasound in diabetic pregnancies (1) to birth weight; (2) to other sonographic markers of diabetic fetopathy (expected fetal weight, sectional area, and fractional volume in fetal limbs); and (3) to maternal biochemical markers of diabetes(HbA1c, leptin).

Methods: Fetal adrenal gland measurements were obtained between 32 and 34 weeks. The gland length, width, depth, and volume (by Virtual Organ Computer-Aided Analysis [VOCAL]) were measured for total gland and fetal zone. Fetal total and fat sectional area and fractional volume were obtained in arm and thigh. A maternal blood sample was obtained. Univariate and multivariate models were used to assess the associations.

Results: Thirty-nine diabetic pregnancies were included. Birth weight related significantly to total and fetal zone adrenal depth, and total adrenal volume in third trimester. Total adrenal length and corrected adrenal gland volume also showed a significant correlation to birth weight percentile in univariate and multivariate models. Total adrenal volume associated significantly to total and fat areas and volumes in fetal limbs. Both maternal leptin and HbA1c levels found a significant positive relation to fetal total adrenal volume and corrected adrenal gland volume. Total adrenal gland volume showed a significant association to maternal HbA1c level in multivariate model.

Conclusions: An enlargement of the fetal adrenal gland may be observed in gestational diabetes, not only related to birth weight, but also to distinctive features of diabetic pregnancies, such as fat tissue fetal deposits or maternal biochemical markers.

5. **Predictors of caesarean section - a cross-sectional study in Hungary.**

   Rénes L, Barka N, Gyurkovits Z, Paulik E, Németh G, Orvos H.

   J Matern Fetal Neonatal Med. 2017;23:1-18.

Objective: The aim of this study was to analyse the factors associated with caesarean section (CS) at the Department of Obstetrics and Gynaecology, University of Szeged, Hungary.

Study Design: Data collection was based on self-administered questionnaire and medical records related to the deliveries in the year of 2014. Maternal age, education level, marital status, pre-gestational body mass index (BMI), infertility treatment, previous CS, gestational diabetes mellitus (GDM), pre-pregnancy hypertension and pregnancy induced hypertension (HT/PIH) were examined. The participation rate was 67.3%, multiple pregnancies and questionnaires with missing data were excluded (n = 1493). Univariate and multivariate comparisons were performed.

Results: There were 1125 (45.4%) CSs out of 2479 deliveries. CS rate: 40.0%. Underweight 109 (7.1%), normal 921 (60.2%), overweight 320 (20.9%) obese 181 (11.8%).

HT/PIH7.6% (n = 117), GDM: 10.1% (n = 155). The odds of CS were significantly higher among obese mothers (OR: 1.81) compared to the normal weight group. Increasing maternal age (OR: 0.97) and being underweight (OR: 0.59) significantly decreased, previous CS (OR: 12.19), infertility treatment (OR: 1.91) and HT/PIH **(OR: 1.87) significantly increased the probability of CS.**

Conclusions: Pre-gestational obesity, infertility treatment, previous CS and HT/PIH **had significant effect on the mode of delivery.**

6. **Association between polycystic ovary syndrome and the risk of pregnancy complications: A PRISMA-compliant systematic review and meta-analysis.**

   Yu HF, Chen HS, Rao DP, Gong J.

   Medicine (Baltimore). 2016;95(51):e4863.

Objective: The purpose of this meta-analysis was to summarize the evidence regarding the strength of the association between pregnancy in women with PCOS and pregnancy complications.

Methods: We systematically searched PubMed, EmBase, and the Cochrane Library to identify observational studies up to January 2016. The primary focus was pregnancy outcomes, including gestational diabetes mellitus (GDM), preeclampsia, pregnancy-induced hypertension (PIH), preterm delivery, cesarean delivery, oligohydramnios, and polyhydramnios. Effect estimates were pooled using the random-effects model. The analysis was further stratified by factors that could affect these associations.

Results: We included 40 observational studies that reported data on a total of 17,816 pregnancies with PCOS and 123,756 pregnancies without PCOS. Overall, PCOS in pregnancy was associated with greater risk of GDM, preeclampsia, PIH, preterm delivery, cesarean delivery,

miscarriage, hypoglycemia, and perinatal death. However, PCOS in pregnancy had little or no effect on oligohydramnios, polyhydramnios, large-for-gestational age (LGA), small-for-gestational-age (SGA), fetal growth restriction (FGR), preterm premature membrane rupture, fasting blood glucose (FBG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglyceride, total cholesterol, congenital malformation, macrosomia, and respiratory distress syndrome. Subgroup analysis suggested that these associations might be influenced by study design and pre-BMI.

Conclusion: PCOS in pregnancy is associated with a significantly increased risk of adverse pregnancy, fetal, and neonatal outcomes.

7. Obstetric and perinatal outcome in anti-Ro/SSA-positive pregnant women: a prospective cohort study.

Martínez-Sánchez N, Pérez-Pinto S, Robles-Marhuenda Á, Arnalich-Fernández F, Martín Cameán M, HuesoZalvide E, Bartha JL.

Immunol Res. 2017 Jan 30. doi: 10.1007/s12026-016-8888-5. [Epub ahead of print]

Background: Anti-Ro/SS-A is one specific type of antinuclear antibodies. They are in the majority of cases associated with primary Sjögren syndrome (SS) but also in Systemic Lupus Erythematosus (SLE), rheumatoid arthritis (RA), and in healthy people. During pregnancy, they are mainly associated to congenital heart block (CHB) and neonatal lupus (NL). The aim of this study was to compare the rate of maternal and fetal complications between a series of anti-Ro/SS-A positive pregnant women prospectively followed.

Methods: Forty-two anti-Ro/SSA antibodies positive pregnant women that were referred to our hospital between 2011 and 2015. Data about pregnancy follow-up and outcomes were prospectively recorded from electronic databases. Data included demographic characteristics of the patients and their diseases (type, treatments, profile of anti-Ro/SSA, and antiphospholipid antibodies), pregnancy complications (CHB, preeclampsia, preterm delivery), ultrasound examinations and conditions, and mode of delivery.

Results: Maternal age was 35.22 ± 3.42 years and most of them were either SLE (n = 16, 40%) or Sjögren syndrome (n = 15, 37.5%). The rest of them were asymptomatic carriers (n = 8; 20%), and there was only one case of rheumatoid arthritis (n = 1; 2.5%). The incidence of anti-Ro52 and anti-Ro60 positive was n = 13, 82.4% and n = 16, 100%, respectively. Anti-La/SSB antibodies were present in n = 17, 48,6% of the patients. Half of the patients were taking hydroxycloroquine (n = 18, 45%). Seven pregnancies were complicated by fetal anti-Ro-related cardiac disease (17.9%) including four cases (57.1%) of second-degree heart block, two cases of third degree heart block (28.6%) and one case (14.3%) of intense and diffuse hyperechogenicity in atrioventricular valves without heart block. Gestational age at diagnosis of these conditions was 23.2 ± 3.5 weeks. One of the 18 patients having hydroxychloroquine (5.6%) compared with the six of them in women not having this medication (6/22, 27.3%) (p = 0.10).

Concerning about Doppler evaluation, the Z score of umbilical pulsatility index (PI) was significantly higher in the SLE patients (p = 0.02). There were no cases of preeclampsia. Labor was induced in 21 cases (52.5%) and cesarean section rate was 45%. Gestational age at birth was 39 (37-40) weeks, and the general prematurity rate was 20% (n = 8). Birthweight was 2985 g (2425-3185 g) and 2850 (12.25-52.50) centiles for gestational age. The rate of small for gestational age (SGA) infants was 31.3% for SLE patients (5/16), 13.3% for Sjögren syndrome (2/15), and 12.5% for asymptomatic women (1/8). The rate of neonatal acidosis (pH < 7.20) was 20% (8/34) and it was higher in the SLE cases (6/15, 40%) when delivered after 38 weeks.

Conclusions: The main pregnancy complication associated to anti-Ro/SS-A antibodies is CHB. The prevalence of CHB in patients taking hydroxychloriquine is lower without distinguishing between high or low risk patients. Preterm delivery occurs in anti-Ro/SS-A patients at the same rate as in the general population if no complications such as CHB or intrauterine growth restriction (IUGR) occur. The SGA rate also is higher probably because of SLE not because anti-Ro/SS-A antibodies. Finally, the finding of high umbilical artery PI will allow to predict fetus at risk of adverse pregnancy outcomes.

Highlights:

- Anti-Ro/SS-A and anti-La/SS-B are clinically very relevant during pregnancy mainly because of their association to congenital heart block and neonatal lupus.
- In our cohort, the prevalence of congenital heart block detected in patients taking hydroxycloroquine is much lower than in patients not taking it without distinguishing between high and low risk patients.
- High umbilical artery pulsatility index in Doppler scans studies has been detected in our anti-Ro/SSA population (basely in SLE patients) demonstrated this measurement as a predictor of SGA and adverse pregnancy outcomes in general population such as cesarean section for fetal distress. The small for gestational age rate is higher probably because of SLE not because anti-Ro/SS-A
- Preterm delivery happens in anti-Ro/SS-A patients at the same rate as in the general population if no complications such as congenital heart block or intrauterine growth restriction occur.

8. Clonidine versus Captopril for Severe Postpartum Hypertension: A Randomized Controlled Trial.

Noronha Neto C C, Maia SS, Katz L, Coutinho IC, Souza AR, Amorim MM.

PLoS One. 2017 Jan 26;12(1):e0168124. doi: 10.1371/journal.pone.0168124. eCollection 2017.

Background: Changes during the puerperium are still unclear, particularly in women with hypertension. The choice of antihypertensives, both to control very high blood pressure episodes and to keep blood pressure stable, also requires further elucidation. Currently, there are no clear data to guide the decision for the choice of postpartum antihypertensives. Captopril plays an important role in the treatment of very high blood pressure episodes and may be used postpartum. Clonidine has been used as an alternative in pregnant or postpartum women with contraindications to captopril, with satisfactory effect. The objective of the present study was to evaluate the effectiveness and safety of clonidine compared to captopril for treating severe postpartum hypertension.

Methods: A randomized, drug-controlled, triple-blind clinical trial evaluating postpartum women receiving captopril or clonidine. Inclusion criteria consisted of: women with hypertensive disorders of pregnancy **systolic blood pressure (SBP) ≥180 mmHg and/or diastolic blood pressure (DBP) ≥110 mmHg], requiring magnesium sulfate. Exclusion criteria were:** heart disease, smoking, illicit drug use, contraindications to captopril, clonidine or oral medication, and having used captopril/clonidine previously. The primary outcome was the frequency of very high blood pressure episodes while in the obstetric intensive care unit.

Results: A total of 90 postpartum women met the study inclusion criteria, with 45 randomized to each group. There were fewer very high blood pressure episodes during hospitalization (2.1 ± 2.1 vs. 3.5 ± 4.7, p = 0.08), greater percentage reduction in SBP (14.0% ± 8.6% vs. 10.8% ± 8.8%, p = 0.08) and fewer women requiring sodium nitroprusside (2.3% vs. 13.3%; RR: 0.17; 95%CI: 0.02-1.39; p = 0.06) in the clonidine group compared to the captopril group; however, these differences were not significant. The groups were similar regarding daily mean SBP or DBP; however, on the third postpartum day, mean SBP was lower in the clonidine compared to the captopril group (151.9 ± 11.8 mmHg vs. 158.1 ± 13.6 mmHg, p = 0.02). Although not statistically significant, adverse reactions were more common in the captopril group (28.8%) compared to the clonidine group (18.6%).

Conclusion: Clonidine and captopril represent safe, effective treatments for severe postpartum hypertension.

Management of HBsAg positive Pregnant Women - Prevention of Mother to child transmission of Hepatitis B - An Algorithmic approach

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Management of HBsAg positive Pregnant Women– Prevention of Mother to child transmission of Hepatitis B –An Algorithmic approach

- Whether to treat the pregnant woman ?
- How to prevent mother-child transmission?
- Mode of Delivery
- Decide the STAGE of CHB based on the markers

Decide the STAGE of Chronic Hepatitis B based on the markers HBeAg,Anti – HBe Ag, HBVDNA, Serum ALT

Women of childbearing age usually will be in the immune tolerant stage of disease

HBeAg Positive with positive HBVDNA with normal LFT's

Maternal HBVDNA

Immune tolerant
HBeAg Positive with positive HBVDNA with normal LFT's

Immune clearance
HBeAg Positive with positive HBVDNA with high ALT, No antibody

Inactive Hep B carrier
HBeAg negative DNA(<20,000) and raised ALT Positive Anti HBe antibody

CHBReactivation
HBeAg Negative DNA positive with high ALTPositive Anti HBe antibody

Pregnant woman with HBV DNA (<200,000 IU/mL) or 106 copies/ml

Treatment of Mother

No monitoring during pregnancy No need for antiviral therapy

HBIG and HBV vaccine to be given to newborn within 12 h.

Mode of Delivery

In mothers with Low HBVDNA the risk of mother-to-child transmission of HBV during birth remains same whether delivered vaginally or by elective LSCS

Breast Feeding

YES

Pregnant womanwith very high HBV DNA ≥ 200,000 IU / mL or 106 copies/ml

Treatment of Mother

Antiviral therapy should be started from third trimester with Telbivudine or Tenofovir at 28-32 weeks to continue Postpartum with maternal monitoring with HBVDNA (1-2 months interval)

HBIG and HBV vaccine to be given to newborn within 12 h

Mode of Delivery

Elective LSCS in mothers with very high HBVDNA (>10 6 copies/ml) at term or near delivery

Breast Feeding

No if on Retro viral therapy

Yes if Anti retro viral therapy stopped

Risk of transmission with Invasive procedures and obstetric risk factors

No evidence to suggest that amniocentesis or chorionic villus sampling increases the risk of vertical transmission
Inconclusive evidence in Placenta previa, AbruptioPlacenta, Threatened abortion Preterm labor & PROM

KEY POINTS

- Mother to child transmission is an important mode of HBV transmission.
- The rate of chronic infection in the child is much higher (90%) than adulthood transmission (10%–20%).
- All pregnant mothers should be screened for HBsAg during pregnancy. Those positive should be further tested for HBV markers HBeAg, Anti – HBe Ag, HBVDNA and Serum ALT for staging the disease
- HBeAg positivity and high HBV DNA level (>106copies) in pregnant mothers carries a high risk (70%–90%) of MTCT as compared to HBs-positive/HBeAg negative mothers (15%–20%).
- Administration of oral nucleoside analogue (LAM,Telbivudine, Tenofovir) in third trimester in HBs positive mother with very high DNA levels significantly reduces the risk of MTCT.
- Adequate administration of immunoprophylaxis (HBV vaccine + HBIG) within 24 hours of birth is highly effective method to prevent MTCT.
- Breast feeding is not contraindicated in HBs positive mothers to infants who receive complete immunoprophylaxis.

FURTHER READING

1. American Association for the Study of Liver Diseases practice guidelines .Lok AS, McMahon BJ. Chronic hepatitis B: update 2009.Hepatology 2009; 50: 661-662
2. Zhao Zhang, Chao Chen, Zhe Li, Ying-Hua Wu, Xiao-Min Xiao. Individualized management of pregnant women with high hepatitis B virus DNA levels World J Gastroenterol2014 September 14; 20(34): 12056-12061
3. Fan Y, Xiao XM. Meta-analysis on the effect of delivery mode on maternal-infant transmission of hepatitis B virus. ZhongguoFuyouBaojian2007; 22: 3787-3789
4. Yang J, Zeng XM, Men YL, Zhao LS. Elective caesarean section versus vaginal delivery for preventing mother to child transmission of hepatitis B virus--a systematic review. Virol J 2008; 5: 100
5. American College of Obstetricians and Gynecologists (ACOG). Viral hepatitis inpregnancy. In: ACOG practice bulletin; no. 86. Obstetrics and Gynecology 2007; 110: 941–956
6. Lin Ma1, Nageswara R. Alla2, Xiaomao Li1, Ospan A. MynbaevZhongjie Shi1. Mother-to-child transmission of HBV: review of current clinical management and prevention strategies Rev. Med. Virol

"It's not necessarily the amount of time you spend at practice that counts; it's what you put in practice"

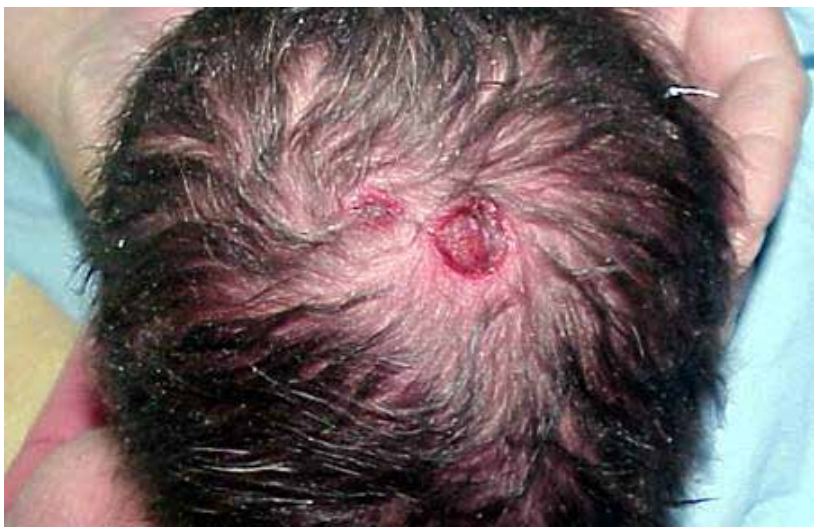
- Eric Lindros

Brain Teasers

Dr. Abha Rani Sinha

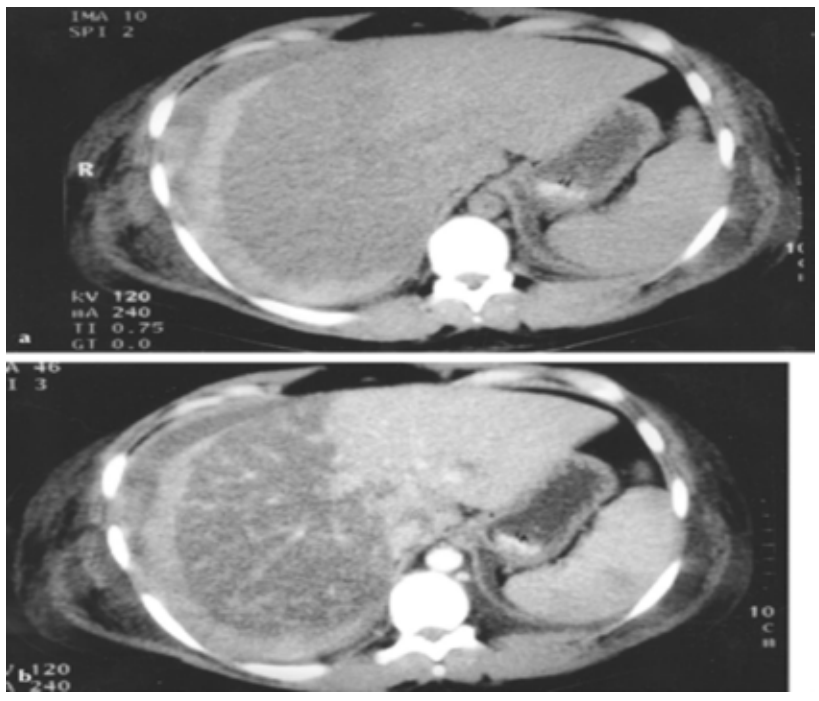
Associate Professor, Obst & Gynae, Patna Medical College, Patna, Chairperson Quiz committee FOGSI (2015-2017)

Q1. This photograph is of a new born baby born to a mother taking some medication for her medical disorder.



- Name this condition.
- Name the drug responsible for it.

Q2. A 30 year primiparous female who had LSCS for severe preeclampsia had severe right upper quadrant pain with deteriorating general condition after 6 hours of delivery,



- What is your diagnosis?

Q3. Risk of Neonatal HIV infection with mother having <400 RNA copies/mL is

(a) 1% (b) 10% (c) 20% (d) 40%

Q4. Single donor platelet transfusion raises the platelet count by……

Q5. Which is the last variable affected by fetal acidosis during biophysical profile scoring

Answers will be published in the next issue.