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Screening for fetal and neonatal alloimmune thrombocytopenia - lessons learned from a Norwegian screening program

Sir,

An important issue on human platelet antigen (HPA)-1a screening has recently been addressed in *Acta Obstetrica et Gynecologica Scandinavia*. Winkelhorst et al. reported that the vast majority of women in the general pregnant population were positive about screening (1). Here we report that there was also a positive attitude towards screening among Norwegian HPA-1a-immunized pregnant women. Further, we report that insufficient information may have led to unnecessary anxiety in this high-risk population.

In the Norwegian screening and intervention study (December 1995- March 2004) , HPA-1a typing of pregnant women was performed using the same blood sample that was collected for routine RhD typing (2) following approvals from the Regional Committees for Medical and Health Research Ethics (Ref. P-REK V 13/95, Dates of approval: February 24th 1995, August 23rd 1998, and September 10th 2001). After identifying the HPA-1a negative women, the participating university hospitals sent a letter to the general practitioners (GP) of these women that included information on fetal and neonatal alloimmune thrombocytopenia (FNAIT) and follow-up recommendations.

A questionnaire was sent to 40 non-immunized and 40 immunized women and their respective GPs; asking for their opinion regarding the screening program. Seventy-five percent non-immunized and 85% immunized women responded. Further, 18 of 40 GPs who were engaged in

the follow-up of immunized women participated in the survey and so did 25 of 40 GPs taking care of the non-immunized women.

Seventy-five percent of the GPs thought it was acceptable to receive results from laboratory analysis that they originally had not requested.

Eighty percent of the non-immunized women and 71% of the immunized women reported that they were not content with the received information. Thus, many women searched for information and pregnancy-related consequences on their own, by either contacting the university hospital, searching the Internet or other sources. Despite of not being appropriately informed, the vast majority of the immunized women (82%) felt that they had been taken good care of during their risk pregnancy.

Half (53%) of the immunized women reported that they probably had been more anxious than they normally would have been during pregnancy, and that the risk status have had implications for their planning of subsequent pregnancies. Of the non-immunized pregnancies, 37% reported they probably had felt more distress during pregnancy than without knowledge of their platelet type, but this had not influenced their planning of subsequent pregnancies.

Our study demonstrated that we had not succeeded in providing sufficient information regarding the screening program and FNAIT, neither to the pregnant women nor to the GPs. Thus, the importance of good communication between specialists in the referral hospital and both the GPs and pregnant women is essential and must be taken seriously when implementation of new screening programs.

Finally, HLA DRB3*01:01 typing (2), quantification of anti-HPA-1a (3), analysis of anti-HPA-1a IgG glycosylation pattern (4) and subtypes (5) as well as non-invasive fetal HPA-1a typing are promising risk stratification tools for future screening programs, which will decrease the number of high-risk pregnancies that need careful clinical follow-up during pregnancy.

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References

1. Winkelhorst D, Loeff RM, van den Akker-Van Marle ME, de Haas M, Oepkes D. Women's attitude towards routine human platelet antigen-screening in pregnancy. Acta Obstet Gynecol Scand. 2017;96:991-997.

2. Kjeldsen-Kragh J, Killie MK, Tomter G, Golebiowska E, Randen I, Hauge R, et al. A screening and intervention program aimed to reduce mortality and serious morbidity associated with severe neonatal alloimmune thrombocytopenia. Blood. 2007;110:833-839.

3. Killie MK, Husebekk A, Kjeldsen-Kragh J, Skogen B. A prospective study of maternal anti-HPA 1a antibody level as a potential predictor of alloimmune thrombocytopenia in the newborn. Haematologica. 2008;93:870-877.

4. Kapur R, Kustiawan I, Vestrheim A, Koeleman CA, Visser R, Einarsdottir HK, et al. A prominent lack of IgG1-Fc fucosylation of platelet alloantibodies in pregnancy. Blood. 2014;123:471-480.

5. Santoso S, Wihadmadyatami H, Bakchoul T, Werth S, Al-Fakhri N, Bein G, et al. Antiendothelial alphavbeta3 Antibodies Are a Major Cause of Intracranial Bleeding in Fetal/Neonatal Alloimmune Thrombocytopenia. Arterioscler Thromb Vasc Biol. 2016;36:1517-1524.