Eight months of experiences in newborn screening for sickle cell disease (SCD) and spinal muscular atrophy (SMA)

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Introduction: Since October 2021, SCD and SMA are included in the German national newborn screening (NBS) panel. Our center started a 3-months NBS pilot study in July 2021. For SCD screening, blood transfusion and prematurity (<34 weeks of gestation) have been announced as major diagnostic pitfalls.

Aim: To report first experiences on prevalence, disease confirmation and diagnostic pitfalls.

Methods: Real-time quantitative PCR (RT-qPCR) investigation of SMA, SCD and TRECs is performed using a common platform to facilitate high-throughput analysis. For SMA screening, the *SMN1* gene is used as a target, while β-actin is used as an internal control for successful amplification. For SCD screening, the common mutation is targeted in RT-PCR. In a second-tier approach for SCD, all samples revealing a suspicious first tier result undergo ESI-MS/MS analysis of characteristic hemoglobin fragments using a commercial kit (*SpOtOn Clinical Diagnostics Limited*).

Results: 84 769 newborns (26 764 within the pilot phase and 58 005 within the regular screening program) have already been investigated. Due to low β-actin levels in 24 cases a control card was requested.
SMA: We identified 13 newborns affected by SMA (birth prevalence about 1: 6 500), 12 of them already confirmed by MLPA (multiplex ligation dependent probe amplification) revealing 0 *SMN1* copies and 1-4 *SMN2* copy numbers, NBS revealed no false positive results.
SCD: We identified 21 newborns with SCD (birth prevalence about 1:4 000): n=17 homozygous Hb S/S, n= 4 compound heterozygotes Hb S/Hb C- confirmation was mostly done by molecular genetics. NBS revealed no false positive results. One recall card needed to be requested due to blood transfusion and three recall cards due to gestational age below 34 weeks (total number of newborns <34 weeks of gestation in the observed period was 3 502, number of transfusions estimated 298).

Conclusion: NBS for SMA and SCD has been successfully established as a Multiplex-qPCR in parallel with the detection of TRECs. In SCD screening, a second-tier approach based on RT-qPCR for the common SCD mutation and subsequent ESI-MS/MS analysis of hemoglobin fragments is feasible and facilitates dealing with the two major pit-falls blood-transfusion and prematurity.