Rapid Genome Sequencing in Critically Ill Children: Current Evidence, Clinical Implementation, and Future Perspectives

Advances in sequencing technologies and analytical pipelines have transformed genomic diagnostics in acute pediatric care. Today, ultra-rapid genome sequencing can deliver provisional molecular diagnoses within 24 hours under optimized clinical conditions, enabling time-critical therapeutic decisions in neonatal and pediatric intensive care units. As a result, rapid genome sequencing (rGS) and ultra-rapid genome sequencing (urGS) are increasingly recognized as first-tier diagnostic approaches for critically ill children with suspected genetic disorders.

This presentation provides an overview of the current international evidence regarding rapid genomic diagnostics in critically ill children. Data from large prospective studies and real-world implementation programs have consistently demonstrated diagnostic yields of approximately 40–60%, with substantial impacts on clinical management, including targeted treatments, avoidance of invasive procedures, optimization of palliative care decisions, and improved family counseling.

The current state of rapid genome sequencing in Germany will be reviewed in the context of recent national initiatives. Particular attention will be given to the implementation of rapid and ultra-rapid genome sequencing within the healthcare system, including experiences from the multicenter Baby Lion study, which demonstrated the feasibility and clinical utility of ultra-rapid genome sequencing across neonatal and pediatric intensive care settings. Furthermore, the role of the German national genomic medicine initiative (Modellvorhaben Genomsequenzierung) in expanding access to genomic diagnostics and establishing sustainable structures for precision medicine will be discussed.

Finally, future perspectives at the interface of acute genomic diagnostics and population-based genomic screening will be explored. While rapid genome sequencing addresses the urgent diagnostic needs of critically ill children, genomic newborn screening aims to identify actionable genetic conditions before symptom onset. Rather than competing approaches, both strategies may represent complementary components of a future genomic healthcare framework, spanning the continuum from early disease detection to precision diagnostics in acute care.