## Study project on stroke in Saudi children

## Conclusions, recommendations and acknowledgments

Mustafa A. Salih, Dr Med Sci, FRCPCH, Abdel-Galil M. Abdel-Gader, PhD, FRCP, Ahmed A. Al-Jarallah, MBBS, ABP.

## **CONCLUSIONS AND RECOMMENDATIONS**

- I-1 This retrospective and prospective study, which spanned 10 years and 7 months, is one of the largest cohorts of children with stroke at one medical center worldwide.
- I-2 Among the study group of 104 Saudi children, ischemic stroke accounted for most cases (82%), whereas intracranial hemorrhage was less common (18%). The relative paucity in the proportion of hemorrhagic stroke, compared to other international studies, may partly be because children with, for example, hereditary bleeding disorders succumb before they manage to reach the secondary or tertiary care hospitals.
- I-3 The present study strongly highlighted the importance of prothrombotic disorders as a risk factor for stroke in Saudi children. No previous study is available where the role of prothrombotic conditions in the pathogenesis of childhood stroke was explored, in either Saudi Arabia or the Middle Eastern Region.
- I-4 Prothrombotic disorders were significantly detected more in the Prospective Study Group than in the Retrospective Study Group. This emphasized the importance of availability of an adequate coagulation laboratory service in the investigation of childhood stroke.
- I-5 Large prospective follow-up studies are needed to evaluate all children with stroke, for prothrombotic conditions and investigate their families if hemostatic abnormalities were identified. Such an approach will ensure that more children will benefit from the appropriate specific treatments designed to prevent stroke and its recurrence.
- I-6 Contrary to previous similar studies from Saudi Arabia, sickle cell disease (SCD) accounted for greater than 10% of the ascertained risk factors and had severe manifestations, highlighting the severe phenotype of SCD which is also prevalent in Saudi Arabia in addition to the mild type.
- I-7 More efforts should, therefore, be focused in elaborating sustained programs aimed at the primary prevention of SCD, through health education and pre-marital diagnosis.
- I-8 Transcranial Doppler (TCD) screening made a significant impact in identifying cerebrovascular disease associated with SCD. This non-invasive and less technically demanding technique needs to be made available at the health centers and hospitals, where patients with SCD are managed. The availability of TCD potentially allows for the primary prevention of stroke through early intervention with therapies, such as regular blood transfusions and hydroxyurea.
- I-9 Acute bacterial meningitis is an important potentially preventable cause of childhood stroke. Immunogenic vaccines against the 3 most common organisms (*Haemophilus influenzae type b*, *Neisseria meningitidis* and defined types of *Streptococcus pneumoniae*) are also needed to cover the young (<2 years) who are mostly affected.
- I-10 The study described the first reported cases of stroke as a manifestation of neurobrucellosis, and suggested that investigation for neurobrucellosis should be part of the diagnostic work-up in Saudi Arabia and other similar countries of the Region.

- I-11 Congenital toxoplasmosis and rubella syndrome were also identified risk factors for childhood stroke. Both are potentially preventable through immunization, other maternity health programs, or both.
- I-12 Congenital and genetic cerebrovascular anomalies are also important risk factors. Prompt diagnosis and neurosurgical intervention may be life saving in these conditions.
- I-13 Underlying cardiac anomalies should be excluded in cases of childhood stroke, since these conditions can be asymptomatic, as has been the case in one patient in this cohort.
- I-14 Moyamoya syndrome (MMS) is a significant underlying cause of stroke in Saudi children. It was found to be associated with another disease in all identified cases. The association of MMS and protein C deficiency was first reported in this cohort of patients, whereas the associations of the syndrome with wrinkly skin syndrome (OM1M 278250) and Adams-Oliver syndrome (OM1M 100300) have not, hitherto, been described. Revascularization surgery (encephaloduroarteriosynangiosis) is a safe intervention method even in patients with hypercoagulable disorders (protein C deficiency) and in SCD.
- I-15 Inherited metabolic disorders (all due to underlying mitochondrial disorders in this cohort) caused stroke in 3.8%. Specialized reference laboratories are required for the proper investigation of these cases, as a prerequisite for genetic counseling aiming at the prevention of secondary cases.
- I-16 Hypernatremic dehydration contributes to stroke in Saudi population. The condition can be effectively controlled by health education to encourage breast-feeding and the universal use of oral rehydration solution at the primary health care level.
- I-17 Post-traumatic arterial dissection requires a high index of suspicion and adequate neuroimaging facilities for diagnosing the condition. When identified, recurrences can be curbed by appropriate therapeutic interventions.
- I-18 The outcome of stroke in Saudi children constituted a huge burden with a high rate of motor, cognitive and language deficits. Residual epilepsy affected 58%. The socio-economic consequences for the victim, family, and the community at large are challenging. Programs aiming at the primary prevention of the causes of stroke remain the corner stone in reducing the burden of childhood stroke on the health service and the society.
- I-19 Because of the high prevalence and importance of multiple risk factors, complete investigation, including hematologic, neuroimaging and metabolic studies should be considered in every child with stroke.
- I-20 Based on the experience gained from this study and the international guidelines, a diagnostic algorithm outlining the approach to a child with a suspected stroke/cerebrovascular lesion, was formulated. The algorithm might also be of use for managing other children from the Arabian Peninsula and Middle Eastern Region, with similar demographic, socio-economic, and ethnic backgrounds.
- I-21 Nationwide, handling childhood stroke can be achieved effectively by the development of specialized stroke care services, designing and implementing a childhood stroke registry via the Internet, and the efficient use of Telemedicine to help in the initial management of patients at various district and regional hospitals.

## **ACKNOWLEDGMENTS**

The Investigators are greatly indebted to the Prince Salman Center for Disability Research (PSCDR) for the generous grant (Project No. B/M/4/15), without which this work could not have been possible. The kind and dedicated support from HRH Prince Salman bin Abdulaziz Al-Saud, President of the PSCDR, and HRH Prince Sultan bin Salman bin Abdulaziz Al-Saud, Chairman of the Board of Trustees, Executive Directors, and Administrators of the PSCDR kept it thriving throughout the years. We sincerely thank all of them on behalf of children afflicted with stroke in Saudi Arabia, the Region, and Worldwide, who might benefit from the recommendations derived from this work.

We are also grateful to the Vice Rector for Higher Studies and Research, King Saud University, and his Advisors, the Dean, Vice Deans, College of Medicine and Director of the College of Medicine Research Center for their kind help and encouragement. Our grateful thanks also go to the Chairmen of the Departments of Pediatrics and Physiology, College of Medicine, for their continuous support and encouragement.

We also extend our sincere thanks to many scientists, colleagues, doctors, technical personnel, and nursing staff who have been instrumental in the successful completion of this work. These were spread over many

institutes in Saudi Arabia (King Khalid University Hospital [KKUH], King Abdulaziz Medical City/King Fahad National Guard Hospital, and Riyadh Al-Kharj Hospital Program, Riyadh).

Special thanks are due to the colleagues at the Pediatric Neurology, Pediatric Hematology, and Pediatric Intensive Care Units; Division of Neuroradiology, Department of Diagnostic Imaging; Department of Nuclear Medicine; the Divisions of Neurosurgery and Vascular Surgery, Department of Surgery; Department of Biochemistry; and the Divisions of Immunology, Histopathology, and Microbiology, Department of Pathology, College of Medicine, King Saud University, Rivadh for their valuable contributions.

We gratefully acknowledge the kind help offered by several international institutes for the biochemical, molecular biological analyses, or both, needed for patients with suspected mitochondrial disorders. We feel indebted to Professor Salvatore DiMauro and Dr. Arthur P. Hays, Columbia University, New York, USA; Professor Massimo Zeviani, Division of Molecular Neurogenetics, National Neurological Institute, Milano, Italy; and Dr. W. Ruitenbeek, Laboratory of Pediatrics and Neurology, University Medical Centre Nijmegen, Nijmegen, The Netherlands.

The technical help of the staff of the College of Medicine Research Center, King Saud University is greatly appreciated. Special thanks are also due to Dr. Adbullah H. Abu Jamea, MRI Unit Supervisor, KKUH for the dedicated help he offered for the patients, and for helping with computation and editing of the neuroimages. Thanks are also due to Loida Manalo for her excellent secretarial assistance and for typing the report, and Ver Salvador for the medical illustrations. The secretarial help of Abdulbasit Jalal is thankfully acknowledged.

Finally, we thank our families and all our friends who believed in our work and encouraged us during the long, hectic, and demanding years.