Dr. Sandhya Ghosh Memorial Oration

The case for dedicated sickle cell centres

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Introduction

Sickle cell disease is an inherited blood condition resulting from the inheritance of abnormal genes from both parents. The prevalence of the disease at birth is therefore determined by the frequency of the sickle cell trait in the population. Since the sickle cell gene in north and south America, the Caribbean and Europe is usually seen among Peoples of African origin, it is commonly believed to be associated with African ancestry. There have been at least three independent occurrences of the sickle cell gene in Africa, known as haplotypes and named after the areas where they were first described: Benin, Central African Republic or Bantu and Senegal. However, a fourth independent occurrence of the sickle cell mutation occurred in Asia and is shared by peoples in the eastern Provence of Saudi Arabia and throughout central India and is known as the Asian haplotype. Sickle cell disease of the Asian haplotype is associated with high levels of fetal hemoglobin and frequent deletional alpha thalassaemia, both factors likely to ameliorate the disease and change the clinical features. Furthermore, malaria is a further factor likely to influence expression of the disease.

In India, the sickle cell gene has been reported in 73% of studies among tribal people, 17% among lower castes, 9% among middle castes and 1% among higher castes.[ii] The tribal foci with sustained high frequencies of the sickle cell trait include the Irula/Kurumba/Paniyan in Tamil Nadu with prevalences up to 40%, the Gonds in Andra Pradesh, Madhya Pradesh, Chhatisgarh, Maharasta, Orissa and Uttar Pradesh with prevalences up to 34%, the Bhils in Madhya Pradesh, Chhatisgarh, Maharasta, Gujarat and Rajastan with a prevalence up to 31% and the Kolaran in Maharasta and Gujarat with a prevalence up to 18%. Many assumptions have to be made in predicting the prevalence of patients with sickle cell disease but with a 20% trait frequency, 1% of births would have homozygous sickle cell (SS) disease or 10,000 cases per million population. This would equate to 500,000 cases of disease among a population of 50M or 1M cases for an at-risk population of 100M. These figures suggest that the disease in India is at least as prevalent as in Equatorial Africa. Considering the life-long care needed for patients with a genetic condition, this would represent a huge burden on the health care services.

Whether the disease occurs in India, Africa, south or north America, the Caribbean or Europe, a case could be made for delivery of health care through dedicated Sickle Cell Centers.

1. Need for a seamless service. Sickle cell disease is a life-long condition in which patient and family require continuous care and education. Currently clinical care is usually organized into pediatric and adult services with transition occurring at some time between 12-18 years. On reaching an arbitrary age, children are asked to leave the care of their pediatrician who has followed them throughout childhood and attend different physicians at a different time and a different place. This decision is made regardless of the maturity of the child, which is frequently delayed in SS disease. As a result, many default from follow-up at the critical time of adolescence, when they suffer many problems of the disease such as enuresis, delayed maturity, educational problems at school and increasing leg ulcers and painful crises. The present system does not serve sickle cell patients well and may be solved by a dedicated center offering a familiar setting with the same nurses, technologists, counselors but only a different physician at the time of transition.

2. Specialist sickle cell physicians. The disease itself is characterized by accelerated red cell breakdown causing anemia, jaundice and gallstones and the

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abnormal red cells block flow in blood vessels causing a multitude of clinical symptoms such as stroke, serious chest problems, recurrent bone pain, leg ulcers, bone infections and joint damage, loss of vision, splenic problems and susceptibility to infection. These problems can be addressed by multiple independent specialists, which may inconvenience patients having to attend multiple clinics at different times and places but also carries the danger that no individual physician maintains overall supervision of the patients’ clinical needs. An alternative could be provided by specialist sickle cell physicians with experience in the clinical complications of sickle cell disease. Such physicians require expertise in many areas of clinical care including hematology, pain management, leg ulcers, adolescent medicine, renal problems and psychiatry. They will also have to provide education and support for the patient and their family. With so many areas of specific pathology, advice will be sought from a variety of specialist physicians and surgeons and coordination of these activities will also be needed. Specialists in orthopedics, ophthalmology and urology will be required but such interventions should be conducted within a coherent treatment plan. The bone and eye problems of sickle cell disease require particular expertise and results are likely to be better with surgeons with special experience in the disease, which could be provided by a dedicated center.

3. Diagnostic and hematological services. The differential diagnosis of sickle cell disorders, the vital distinction from the sickle cell trait and the differentiation of less common sickle cell syndromes are more accurately performed in laboratories with specialist expertise. Reticulocyte counts are vital in the management of hematological complications and although simple to perform, may not be rapidly or readily available in routine laboratories. Some specialist techniques such as estimation of fetal hemoglobin (HbF) and serum folate may be useful. Furthermore, rapid results are more easily achieved by a dedicated laboratory and preferably the hematology should be available at the time of clinical consultation, especially for the diagnosis of the aplastic crisis and some other complications. DNA technology necessary for prenatal diagnosis and valuable for research may be more easily developed and monitored within specialized units.

4. Regular review of all patients. Many patients with sickle cell disease are well much of the time and only attend doctors when complications develop. There is now increasing evidence that close monitoring of patients during the steady state (that is, when clinically well) provides baseline data valuable in interpreting complications when they occur. Regular review of the steady state may detect complications not yet clinically apparent and allow earlier intervention. Such review also provides a better time for developing the relationship between patient and physician without the pressures of acute clinical problems. Not only a better relationship, but often more revealing histories may be obtained and chronic concerns or problems such as depression, which commonly complicates sickle cell disease, may be addressed. Within the context of regular review, patients are encouraged to present early with complications and such review provides a better time for education of patient and the family.

5. Day-Care Facilities. Pain management on an outpatient basis provided through day-care facilities has greatly reduced the demands for hospital admission reducing costs and providing a more patient-friendly option for painful crises. The provision of outpatient beds has been invaluable for providing transfusions and for the better, more acceptable management of the painful crisis. The latter accounts for 60-80% of sickle-related hospital admissions in the UK and the US and in both countries is viewed by patients as a major deficiency in management, most patients having to attend Accident and Emergency Departments of busy hospitals, where their painful crisis may have to contend for management with life threatening situations such as bullet wounds and car accidents. The result is a perceived hostility from the medical and nursing staff and an atmosphere, sensed by the patients, to lack the sympathetic support helpful in the resolution of bone pain. The result is that patients tend to defer attending emergency services until the pain is unbearable with resulting distress and distrust. In Jamaica, most painful crises follow a skin cooling-induced avascular necrosis of bone marrow and do not represent an intrinsically serious pathology. In this situation, day-care management has been welcomed, was much preferred by patients and provided savings in inpatient costs.

6. Database management. The large amounts of clinical and hematological data accumulated during the
management of large numbers of patients over long periods make mandatory some form of database system so that results can be readily interpreted and be made available for patient management. Database systems specifically designed for sickle cell patients are available expediting clinical management and research. These systems may detect trends such as the gradual fall in hemoglobin associated with the onset of chronic renal failure and real time plotting of height detects the growth failure and crossing of centiles which may strengthen the indication for splenectomy in chronic hypersplenism. They are also invaluable tools for clinical research making available lists of subjects with specific complications or features required for study. Furthermore, they can maintain ‘housekeeping’ functions, such as the time distribution of future appointments, tracking defaulted patients, patterns of prescribing and stored samples available in serum and DNA banks.

7. Clinical research potential. In the interests of improved management of the hematological and clinical features of the disease, clinical and basic research into new interventions should be conducted. The establishment of a single center simplifies the conduct of research protocols and the center database is available for clinical research. Such a database provides the potential for study of specific complications such as avascular necrosis of the femoral head, priapism and postpriapism impotence, leg ulceration, stroke, acute chest syndrome and delayed physical and sexual development. Greater numbers allow the application of epidemiological and statistical techniques not previously possible and which may be powerful tools for understanding clinical and hematological risk factors for complications.

8. Specialist training. The expertise available within a dedicated center provides the infrastructure for the training of specialist nurses, technologist, counselors and physicians. The need for specialist training in the management of sickle cell disease is increasingly acknowledged and will contribute to better and more effective clinical management. Physicians with less experience may resort more frequently to blood transfusion, hospital admission and surgery for which there are no clear supporting data, exposing the patients to unnecessary risks and using resources which may be better deployed in other ways. There is an urgent need for expertise in the management of sickle cell disease and also training structures, which will allow doctors to pursue careers in sickle cell disease and provide the continuity important in clinical care.

9. Educational and counseling services. The simple inheritance patterns make this condition suitable for premarital counseling and for advising partners in established relationships who both carry abnormal genes. Education is also vital for families with affected children and for the patients themselves in order to better manage their disease. Greater understanding of the precipitating factors for painful crises may avoid many events; parents and teachers need to know what symptoms are potentially serious and which may be safely managed at home or at school. Education of the parents ‘empowers’ them to cope better with their children avoiding panic and insecurity, which is transmitted to the child. This information may be conveyed by the development of specific educational materials such as posters, pamphlets and books, as well as video demonstrations. A dedicated center provides a focus for such educational materials which may be displayed on walls, available from tables and played on video monitors in the waiting areas.

It would be inappropriate to assume that a single model of health care for sickle cell disease would apply to all societies and the review above derives from experience in the development of sickle cell services and clinical research over the last 40 years in Jamaica. However, this review is also informed by interaction with many patients in more developed countries where despite sophisticated laboratory, diagnostic and basic research facilities, the services may fail in providing the informed medical staff and continuity of care sought by many patients. In Africa and in India, both characterized by huge numbers of patients and limited investigatory and diagnostic facilities, it is hoped that the proposed model of care may provide a basis for developing specialist centers. These could perform clinical research and develop and test locally appropriate models of care, which may then be implemented on a broader basis. At the least, this review should provide a basis for such debate.

References

A Brief Biography of Dr. Sandhya Ghose

It is with no mean pride that while charting the illustrious career of Dr. Sandhya Ghose, we begin by saying that she commenced her medical studies and obtained her first medical degree from this very Medical College of Calcutta. It was more than a kind destiny that brought her to this profession. Her father, the late Dr. K.B. Ghose, Professor of Radiology at her alma mater, must have been an inspiration as well. Receiving her M.B.B.S. degree in 1955 she went on to work for her doctoral studies, under the able guidance of the late Prof. J.B Chatterjee, then at the Calcutta School of Tropical Medicine. The year 1964 turned out to be a fruitful one for Dr. Ghose as she gained her Ph.D. on “Acute Myeloid Leukaemia” and had the distinction of becoming a Fellow of The International Society of Haematology.

If Dr. Ghose had proved herself a conscientious and brilliant student, her career in public service was by no means to lag behind. Her first assignment on joining Nilratan Sarkar Medical College was to create a Haematology department from the scratch. Her work there was to prove a lasting contribution to health sector services in West Bengal. In the year 1974, Dr. Ghose traveled to the United Kingdom where she was a clinical observer in Hammersmith and St. Thomas Hospital. She also had the good fortune to meet the celebrated Prof. G.I.C. Ingram in a professional capacity there.

On her return, she joined the Medical College, Calcutta and took charge of the Haematology unit there. As Associate Professor of Medicine and Head of Haematology department, she led many a radiant mind to fruition. Two of the leading Haematologists of the present day, namely the Director of this Institute, Prof. Utpal Chaudhuri and Prof. Moloy Kumar Ghose, Head of the Haematology unit of Nilratan Sarkar Medical College blossomed under her tutelage. Retiring from nearly three decades of active service in 1995, she continued to function as a leading consultant Haematologist until her demise on the 25th of January 2002.

Though one is apt to judge Dr. Ghose’s career exclusively from a medical point of view, one cannot but mention the million facets of her character that made her a cut above the ordinary. A student of the Sarod maestro Radhikamohan Moitra, she was an exponent of the highest originality, as well as a Radio artist of long standing. Though shy of public accolades she was fiercely devoted to her work and students and would brook no obstacle to stand in her way. An exemplary student, an assiduous and innovative teacher and an exacting administrator she had the rarest of gifts. She was beloved of all, because she loved all. This basic humanist temper of Dr. Ghose shines through everyday even though she is not with us anymore. May her soul have peace everlasting.

Dr. Sandhya Ghose received her first medical degree from the Medical College of Calcutta, where her father the late Dr. K. B. Ghose was Professor of Radiology. After qualifying MB, BS in 1955, she pursued post-doctoral studies with the late Professor J. B. Chatterjea at the Calcutta School of Tropical Medicine. In 1964 she was awarded a PhD for her work on acute myeloid leukaemia. She then created the Department of Haematology at the Nilratan Sarkar Medical College in West Bengal and in 1974, travelled to the United Kingdom to work with Professor GIC Ingram at St. Thomas’ Hospital in London. On her return to Calcutta, she joined the Haematology Unit at the Medical College of Calcutta where two of her students included Professor Utpal Chaudhuri, Director of the Institute of Haematology and Professor Moloy Kumar Ghose, head of the Haematology Unit of the Nilratan Sarkar Medical College. Retiring in 1995, she continued as a leading Consultant Haematologist until her demise on January 25, 2002.

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