SQU Med J, May 2012, Vol. 12, Iss. 2, pp.133-136 , Epub. 9th Apr 2012
Submitted 14th Jan 12
Accepted 17th Jan 12

EDITORIAL

Deaths from Sickle Cell Disease in Intensive Care Units

Can we do better?

Lamk Al-Lamki

الوفيات الناجمة عن مرض فقر الدم المنجلي في وحدات العناية المركزة

هل نستطيع عمل ما هو أفضل؟

لمك اللمكي

In this issue of the journal, Dr. Qutaiba Tawfic and his colleagues report their experience with sickle cell disease patients (SCD) who were admitted to the Intensive Care Unit (ICU) at Sultan Qaboos University Hospital, Oman, with various complications of sickle cell disease. They studied 49 patients who were admitted 56 times in the ICU between the years 2005 and 2009.[1] This is an important study which has several points worthy of reflection. There is very little literature specifically discussing the subject of SCD patients who are admitted to an ICU for any SCD related complication. The literature typically deals with specific complications of SCD, like the acute chest syndrome (ACS), vaso-occlusive disorder and stroke in these patients, as well as their precipitating factors and their management.[2–5]

The mortality among Tawfic *et al.*'s, patients admitted to the ICU was 16%. They pointed out that this figure was lower than the general mortality rate of 21.1% in that ICU.[1] However, this is not much of a consolation, and it is far from being a reason to rejoice. A typical patient admitted to an adult ICU, for problems other than SCD, is generally older than the patients who were the subject of this study. Patients in this study had a median age of only 27 years and the oldest patient was 52 years old. Therefore, the mortality of these patients cannot be compared to the mortality of the general adult ICU patients. The 16% mortality rate is indeed alarming for such a young population and should not be readily accepted. It should be a wake-up call as here we are dealing with a hereditary blood disorder, a killer disease of young adults. The situation is probably much worse than that if we include the number of children dying from complications of SCD in paediatric ICUs across this country, and in the general medical and paediatric wards. Child statistics were not included in this study, which only investigated adults SCD sufferers admitted to the ICU. The number of children who die in Oman from SCD is not clear and needs further studies. How many other children and adults die from SCD in their homes in Oman? We truly need to exert a more concerted effort to find out the basic facts about this disease in Oman. Medical researchers need to stop and ponder about the impact of this devastating disease on our society. This needs the full attention of the government in general, the health services in particular and more expectations from patients and non-governmental organisations (NGOs). We need answers!

Unfortunately, in the Western world, SCD is relatively rare and, hence, there is limited interest in research into this disorder. As a result of the low incidence, it has neither drawn the attention of researchers nor stimulated pharmaceutical companies to fund SCD research. There were

Editor-in-Chief, SQU Medical Journal, College of Medicine & Health Sciences, Sultan Qaboos University, Muscat, Oman.
**E-mail: mjournal@squ.edu.om*

a number of clinical research studies on SCD published from the United States in the 1990s, many of them in reputable journals like New England Journal of Medicine,[4,5] and other Western journals, but there were very few basic research studies into this disease. This was followed by a relative lull in the 2000s, when there was even less research published on the subject. Interest had probably waned for above-mentioned reasons. Earlier clinical research on SCD was into the major complications such as ACS, vaso-occlusive disorder, fat embolism, etc. and how to manage them. Unfortunately, these studies, though worthwhile, contributed little to the basic understanding that is needed to reduce SCD mortality in countries such as Oman where it is prevalent. Thus, Oman and the other Arab countries need to be more proactive and themselves undertake research into inherited blood disorders such as SCD. This would ultimately reduce not only mortality and morbidity, but also lessen the social and cultural impact of these diseases. For example, relationships can be disrupted and marriage plans destroyed because of the fear that a potential partner has the sickle cell trait or disease.

Tawfic *et al.* have shown that ACS is the most common cause of death in their group of patients. This is not an altogether new finding, but nonetheless interesting. It is well known that ACS is the second commonest cause of SCD admissions after painful crisis, and it is the prime cause of death killing around 30% of SCD patients. Even though ACS was described approximately 20 years ago,[2] and repeatedly studied by others,[3,4] we have not advanced much in either managing this condition, preventing it or dramatically reduce its effect, at least not in Arab countries. An aetiological contributing factor to ACS is fat embolism, yet little research is gone into preventing or combating that condition, although there is some evidence that hydroxyurea can reduce the recurrence of ACS, and reduce its severity.[6]

Other patients die of acute stroke, commonly a result of vaso-occlusive disease. Again, we physicians as the health guardians of our communities have failed our societies by allowing ourselves to remain in the dark with respect to the disorders that lead to fat embolism, vaso-occlusive disorders, acute stroke and ACS, or other complications of SCD. We have achieved some progress in infection control, which is another major contributing factor to the mortality of SCD, and we do use the current preventative treatment with hydroxyurea.[7] All these complications were present in the patients studied by Tawfic *et al.*

In the USA, the prevalence of heterozygous carriers of the sickle cell trait is 8% among the African Americans.[8] This has lead Bruce Mitchell to summarise the frustration on the current lack of relevant SCD research in USA very concisely: "That is where we are: inconclusive data have been accepted; inconsistent messages about screening, prevention and precaution have been relayed; and research into sickle cell trait-associated sudden death has not advanced. For many physicians, the story stops there."[8] Typically, patients with sickle cell trait have about 40% of their haemoglobin as haemoglobin-S, but they do not have anaemia and so are able to live a normal life. Unfortunately, that is not always the case in Africa where life expectancy of the 6 million people with sickle cell anaemia is only half the normal life expectancy.[9] The World Health Organization (WHO) has declared SCD a public health priority. "The WHO estimates that 70% of sickle cell anemia deaths in Africa are preventable with simple, cost-effective interventions, such as early identification of sickle cell anemia patients by new born screening and subsequent provision of comprehensive care such as giving regular prophylaxis such as penicillin V and vaccinations. Implementation of comprehensive care for SCD patients could lead to improved survival through these targeted interventions."[9] If 70% of SCD deaths are preventable in Africa with simple interventions, then we should be able to achieve a higher percentage in Oman with all the resources and potential that we have in Oman. If the WHO has declared sickle cell disease a public health priority in Africa, then why is it not one here in Oman? Certainly, we need to pause and ponder—what do we need to do in Oman for this public health priority and to reduce the mortality?

To start with we need early detection of the trait and of the symptoms of the disease. In Africa, haemoglobin-S trait is protective against malaria, morbidity and mortality, and hence, to some extent, it may protect some people from that disease.[10] Although it may be that the sickle cell gene has come to Oman for the same reason, this country no longer has a major problem with malaria and therefore we can afford to rid of SCD. The prevalence of SCD in

Oman is generally accepted as 6%.[11,12] The incidence of the sickle cell disease itself has been reported at both 0.2%.[12] Clearly, we need much more research to obtain more accurate statistics on both, the trait and the disease. Recent prospective data from our university hospital and Sohar hospital by AlKindi *et al.* indicates the incidence of SCD is about 0.3%.[13]

The Oman Hereditary Blood Disorder Association was established with the aim of improving services provided to patients with haemoglobin disorders in Oman, including on psychological and social levels.[11] They raise awareness about hereditary blood disorders, including SCD, and their effects on the community. This Association involves both health professionals and patients and, while they are doing a commendable job, they need to be more active in lobbying for legislation on widespread testing and screening for hereditary blood disorders, and in calling for more research. The Research Council (TRC) of Oman is currently supporting one on-going research project on SCD. However, as we have seen, with a mortality rate of over 16% from SCD in one Omani ICU, we need much more basic research on the aetiology and management and, specifically, prevention of all the complications. The Association needs to work in concert with the Research Council and the Ministry of Health to reduce this mortality.

Western countries such as USA and UK have managed to lower their overall mortality from SCD (not only in the ICU) from 3% to 0.13 per 100 person years of observation.[9] Surely, we need to do even better because of the impact this condition has on our society. Our doctors have the know-how but we need more support from the NGOs, the public and the Ministry of Health. Oman is spending one of the lowest percentages of gross domestic product (GDP) on health care, compared to most of the world—only just over 2% of GDP, compared to 6–12% in other countries and 17.4% in the USA.[14,15] Oman needs to invest more money to support and improve our health system and reduce mortality from SCD and other hereditary blood disorders. Our health care investment levels should not remain at about the lowest in the Gulf region, and much lower than most other countries.

So what is the effect of this low health care expenditure on SCD? To start with, if we had more ICU beds, then we might be able to admit patients earlier and therefore, reduce mortality. As indicated above, because there is very little in the world literature on ICU patients with SCD, we have no statistics to compare with our figure of 16% mortality, but general medical logic tells us that we should be able to lower this rate by earlier intervention and better preventative measures. Not only should doctors and the ministry be more vigilant, but also, the patients need to be better educated about the disease, e.g. by presenting themselves early to the doctor, as soon as they have symptoms that may suggest ACS, such as fever, shortness of breath or cough.

The paper published in the New England Journal of Medicine in 1994 studied 538 patients with SCD and ACS.[4] Their mortality was lower with only 18 out of their 538 patients dying from ACS (3.3%). Certainly, this would indicate that mortality from ACS can be reduced with adequate and early medical intervention which implies greater expenditure and investment in our health services.

In 1999, the National Institutes of Health in the USA published suggestions for preventing morbidity and mortality from SCD, from which we could learn several lessons and develop more research.[16] Likewise, the Harvard study[17] and the Sultan Qaboos University studies[18,19] also offer some ideas which, hopefully, could stimulate the Oman Hereditary Blood Disorder Association and The Research Council to get together and do some similar research on SCD. Overall, we need much more research on this genetic disorder, like many other genetic disorders in Oman and in the Arab world.[20] We have to shoulder this responsibility ourselves as we cannot wait for, or rely on, pharmaceutical companies or Western countries to do this research for us. Yes, we can, and we must do better in Oman.

References

1. Tawfic QA, Kausalya R, Alwan DM, Burad J, Mohamed AK, Narayanan A. Adult sickle cell disease: A five-year experience of intensive care management in a university hospital in Oman. Sultan Qaboos University Med J 2012; 12:177—83.
2. SC Davies, AA Win, PJ Luce, JF Riordan, M Brozovic. Acute chest syndrome in sickle-cell disease. Lancet 1984; 323:36–8. Doi: 10.1016/S0140-6736(84)90193—4
3. Maitre B, Habibi A, Roudot-Thoraval F, Bachir D, Belghiti DD, Galacteros F, et al. Therapeutic approach, outcome, and results of BAL in a

monocentric series of 107 episodes. Chest 2000; 117:1386–92. Doi: 10.1378/chest.117.5.1386

4. Vichinsky EP, Neumayr LD, Earles AN, Williams R, Lennette ET, Dean D, et al. Causes and outcomes of the acute chest syndrome in sickle cell disease. National Acute Chest Syndrome Study Group. N Engl J Med 2000; 342:1855–65.
5. Steinberg MH. Management of sickle cell disease. N Engl J Med 1999; 340:1021–30.
6. Ware RE, Aygun. Advances in the use of hydroxyurea. Hematology Am Soc Hematol Educ Prog 2009:62–9.
7. Steinberg MH, Barton F, Castro O, Pegelow CH, Ballas SK, Kutlar A, et al. Effect of hydroxyurea on mortality and morbidity in adult sickle cell anemia; risks and benefits up to 9 years of treatment. JAMA 2003; 289:1645–51. Doi: 10.1001/jama.289.13.1645.
8. Mitchell B. Sickle cell trait and sudden death -- bringing it home. J Natl Med Assoc 2007; 99:300–5.
9. Makani J, Cox SE, Soka D, Komba AN, Oruo J, Mwantemi H, et al. Mortality in sickle cell anemia in Africa: A prospective cohort study in Tanzania. PlosOne 2011; 6:e14699.
10. Aidoo M, Terlouw DJ, Kolczak MS, McElroy PD, ter Kuile FO, Kariuki S, et al. Protective effects of the sickle cell gene against malaria morbidity and mortality. Lancet 2002; 359:1311–12. Doi:10.1016/S0140-6736(02)08273-9
11. Oman Hereditary Blood Disorder Association. From:http://www.onlinedonations.org.om/donationsportal/Pages/Page.aspx?NID=4836 Accessed Mar 2012.
12. Al-Riyami A, Ebrahim GJ. Genetic blood disorders survey in the Sultanate of Oman. J Trop Pediatr 2003; 49:i1–20.
13. Alkindi S, Pathare A, Al-Madhani A, Al-Zadjali S, Al-Haddabi H, Al-Abri Q, et al. Neonatal screening: Mean haemoglobin and red cell indices in cord blood from Omani neonates. Sultan Qaboos Univ Med J 2011; 11:462–9.
14. World Bank. Health Expenditure as Total % of GDP. From: http://data.worldbank.org/indicator/SH.XPD.TOTL.ZS Accessed Mar 2012.
15. List of countries by total health expenditure (PPP) per capita. From: http://en.wikipedia.org/wiki/List_of_countries_by_total_health_expenditure(PPP)_per_capita Accessed Mar 2012.
16. Olney RS. Preventing morbidity and mortality from sickle cell disease: A public health perspective. Am J Prev Med 1999; 16:116–21
17. Management of Patients with Sickle Cell Disease: An Overview. From: http://sickle.bwh.harvard.edu/scdmanage.html Accessed Mar 2012.
18. Al-Lamki Z, Wali YA, Shah W, Zachariah M, Rafique B, Ahmed S. Natural history of sickle hemoglobinopathies in Omani children. Intern J Ped Hemat/Oncol 2001; 7:101–7.
19. Wali Y, Almaskari S. Avascular necrosis of the hip in sickle cell diseases in Oman. Sultan Qaboos Univ Med J 2011; 11:127–8.
20. Al Ali MT. Centre for Arab Genomic Studies. Genetic disorders in the Arab World – Oman. Editorial. From: http://www.cags.org.ae/cb33for.pdf Accessed Mar 2012.