NVEO
Natural Volatiles & Essential Oils

Impact of Oxidative stress on Sickle cell anaemia patients: A Review

1] Dr. Rina Raibhan Wasnik, 2] Dr. Nilkanth Ramji Akarte, 3] Dr. Archana Dhoke 4]Dr. Ashish. P. Anjankar

1] Asst. Professor, Dept. of Biochemistry, Datta Meghe Medical College, Wanadongri , E- mail : drrinawasnik@gmail.com , drrinapaunipagar@gmail.com Email

2] Prof. Emeritus of Biochemistry , Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Sawangi, Wardha

3) Prof & HOD , Biochemistry Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Sawangi, Wardha Email: drarchanadhok@gmail.com , Mob. No.7218271045

4) Prof ,Biochemistry JNMC Sawangi, DMIMS Sawangi Wardha Email: ashish.anjankar@gmail.com;

Abstract:

Introduction: Sickle cell is a lifelong illness and the blood and bone marrow transplant is the only way to cure the patients considering the other functions of the body. However, there are other different treatments available but they provide temporary solutions and recovery for the patient. The major findings of the study involves that sickle cell anaemia is increasing the risk of high blood pressure and improves the number of complications in pregnancy. The blood clotting during the pregnancy is increasing the risk of miscarriage, premature birth and low birth weight. The prior diagnosis of issues can help manage the health and offer clinical care to cure the patient. However, there are very few chances of diagnosing sickle cell in children and offering treatment. It directly affects the nervous system of the individual and affects the organs of the body. Few studies have highlighted these issues and provided different views for minimizing the impact and factors that lead to such disease.

Aim: The study aims to discuss and identify the impact of oxidative stress on sickle cell anaemia patients

Methods: The secondary data collection method was used for conducting the study related to analysis of the impact of oxidative stress on sickle cell anemia patients. There are various studies were evaluated for collecting the information and offering the better understanding related to the oxidative stress and issues related to the sickle cell. The data was collected from studies conducted after 2014. Various databases were analyzed and compared for collecting the critical information about the sickle cell and gaining the understanding of the issues that faced by the individual.

Conclusion: Pathophysiology is highly influenced in SCD by Oxidative stress .It also plays important role in some of the mechanisms related to excessive levels of cell-free hemoglobin

Keywords: Sickle cell anemia, Oxidative stress, Red blood cells.

Background:

Sickle cell disease:

There are different types of factors that have a direct or indirect influence on the health of humans. Sickle cell anaemia is a disorder that occurs due to inherited red blood cells. The RBC is majorly responsible for maintaining the blood flow and oxygen level in the body of a human. In human body the red blood cells move easily through the vessels. According to Voskou et al., (2015), sickle cell anaemia is affecting the shape of the red blood cells and creates issues in the inflow of the cells to

maintain the oxygen level. The blockage in the oxygen supply is having a significant impact on the working conditions of the human body and leads to several consequences. The major health problems that an individual faces due to lack of oxygen supply involves the episode of pain, anaemia and swelling on hands and feet[1]. In addition to this, frequent infection, vision problems and delaying growth are also affecting the health of the individual. Lacking oxygen is a serious problem but it can be understood and mitigated through proper investigation and treatment. As per the views of van Beers, and van Wink, (2018), the causes that increase the chances of sickle cell anaemia involve a mutation in the gene due to issues either from father or mother. The red blood cell of the patient becomes rigid, sickly and misshapen[2]. The risk factor that is highlighted in both studies of Voskou et al., (2015) and Beers, and van Wink (2018) includes the situation of stroke, acute chest pain, hypertension and organ damage. These studies have provided information related to lung infection which leads to chest pain and creates difficulties in breathing. In addition to this, sickle cell issues increase the blood pressure of individuals that lead to paralysis and effects other body tissues. The findings of studies show that sickle cells block the blood flow to organs and deprive the affected organ of blood and oxygen. The major complications of this disorder were identified among adults and children. The lack of oxygen and blood influences breathing and leads to fatigue.

According to Biswal et al., (2019), sickle cell is having a long term impact on the human organ and functional activities. In the current scenario, bone marrow transplant is only considerable way of minimizing the impact of the sickle cell. However, there are other different treatments available but they provide temporary solutions and recovery for the patient. The major findings of the study involves that sickle cell anaemia is increasing the risk of high blood pressure and improves the number of complications in pregnancy. The blood clotting during the pregnancy is increasing the risk of miscarriage, premature birth and low birth weight[3]. Biswal et al. have also analyzed the impact of sickle cells on patients and found that the issues related to the sickle cells are damaging the erection time in men. As per the findings of the study, the sickle cell blocks the blood vessels in the penis which can lead to impotence over time. This kind of condition is increasing infertility in men and affects the intercourse. The major findings of both studies are showing that the sickle cell is a serious problem in the current scenario and influencing the fertility and birth procedure of the humans. Genetic complications among the parents can affect the child and increase the chances of occurrence of sickle cell[4]. The children who have sickle cell disorder by birth have issues related to the lungs, liver and spleen. The prior diagnosis of issues can help manage the health and offer clinical care to cure the patient. However, there are very few chances of diagnosing sickle cell in children and offering treatment. It directly affects the nervous system of the individual and affects the organs of the body. Few studies have highlighted these issues and provided different views for minimizing the impact and factors that lead to such disease[5].

The occurrence of SCD in childhood is leading towards the major complications. It can lead to permanent brain damage or death of the person. The situation of brain damage is occurring due to decrease in the flow of oxygen in blood which results in stopping the brain functions. However, this kind of conditions can be identified considering the body fatigue and low energy. Apart from this the stroke can be occurred without any symptoms. As per the analysis the sickle cell disease can be found at the medium age of 6 years and after 14 years the chances of occurring the disease are more than 8%. As the age of affected child increases the risk of disease improves. In addition to this, Acute Chest Syndrome (ACS) is considered to be a major issue and increase the complications in the body. This is

helping to contribute for high rate of the morbidity and morbidity in SCD. Moreover, these kinds of issues are causing the cavity in lungs that also increase the bacterial infections in organism.

According to analysis, ACS is similar to pneumonia which is likely occurring 50% of the sickle cell patients. The drug related to the cancer named hydroxyurea was used as a chemotherapeutic for curing the patients of sickle cell. Hydroxyurea is majorly used by the medical professionals for treating the patients suffering from sickle cell. This is helping the patient by decreasing the sickle cell haemoglobin polymerization and erythrocyte sickling by increasing fetal haemoglobin (HbF) production, haemoglobin found in newborn babies[6]. Moreover, this drug is highly recommended by the medical professionals for minimizing the impact of body pain and help for preventing from the SCD complications. There are many physicians who are offering this treatment option for most of the patients who are suffering from acute pain episode or symptomatic anemia. According to studies related to the hydroxyurea therapy, the use of medicines like NSAIDs, ibuprofen (Advil or Motrin acetaminophen (Tylenol),), as well as opioids, morphine, oxycodone and codeine are helpful for controlling the sickle cell pain. Opioids can be used for both mild and severe patients that are suffering from sickle cell and acute pain episode. For the children, the screening is one of the most trusted ways of diagnosing the sickle cell disease at the early stage. The medical professionals are advised to use this process for diagnosing the sickle cell among the children.

Impact of oxidative stress:

There are various factors that having direct or indirect impact on the organs and approach of the human related to managing the sickle cell. Oxidative stress is playing a significant role in sickle cell disease (SCD) and associated complications. As per the views of Nader, Romana, and Connes, (2020), oxidative stress is occurring due to the continued production of spices that influence the oxygen level is having a direct impact on the acute inflammation and mechanism for managing the endothelial dysfunction. In addition to this, the mechanism for sickle cell anaemia due to oxidative stress is the chronic pro-inflammatory state. The factors related to haemolysis and chronic inflammation contributes to the production of increased Reactive Oxygen Species (ROS) and affect the health condition of the patient. As per the findings of the study, the patients with HbSS Vaso-occlusive crises (VOC) had a significant level of Hb and a lower mean platelet. The changes in the distribution of platelets have a significant impact on the health and breathing conditions of an individual[7]. The oxidative profile analysis of patients according to the study has suggested that the level of SCD and CAT is higher in the control group as well as the MDA is also playing an important role in the SCD as the changes in the body function might increase the level of other enzyme that influence the organ function of similar trends in the level of a significant case of CAT level were observed in the MDA profile and suggested that the HbSS control group influencing the lung conditions and liver functions of the patients.

The study of Hermann et al., (2016) has also analyzed the impact of oxidative stress on sickle cell patients. According to the study, oxidative stress is occurring due to an increase in the vaso-occlusive crisis and a lowering of the MDA level. HbSS is playing a critical role in the control group patient and affecting the health of the patient. The mutation in the codes of β-globin is increasing the level of oxidative stress and results in substances of different acids like amino, glutamic and protein. These are having a direct impact on the level of blood flow and influencing the health of the individual. These kinds of changes lead to an episode of pain and increase the chance of sickle cell disease. According

to the analysis of different activities of individual, the oxidative stress is one of the major causes for sickle cell disease. The changes in the reactive oxidants is increasing the chances of disorder and planning of the actions[8]. There is higher chance of occurrence of SCD if one of the parents is having such genes. The parents with VOC are having higher changes of occurrence of SCD in their children. The major factors that are influencing the condition of an individual involve chronic inflammation and affecting the level of oxidative stress in the body that leads to sickle cell disease. The comparative analysis of both studies shows that HbSS and MDA levels in the control group are having a significant influence on the occurrence of sickle cell anaemia. The differences in the level of mean corpuscular volume and mean platelets volume is playing a significant impact in the health of an individual. The differences in MCH value and blockage in the blood cells is increasing the problem related to the sickle cell. Both studies have highlighted the role and changes in the HbSS control group that is influencing the liver and lung conditions of the patient suffering from sickle cell. The lower level of CAT and Superoxide Dismutase (SOD) is having a significant impact on the health of an individual. Similar findings of studies involve the oxidative damage and role of reactive oxygen species. The formation of lipid structure and peroxides is having a significant impact on the process of managing the health of the patient of SCD. The changes in the level of MDA among the patients are having a significant impact on the HbSC and affect the genotype partly. Moreover the sickle cell genotype is affecting the concentration of lipid per oxidation.

According to Niihara et al., (2018), sickle cell anaemia is the most common heredity disorder of haemoglobin (Hb) and improvement in oxidative stress is influencing the number of patients in the current scenario. People are facing different issues related to this disease such as pain, tissue ischemia and infarctions. The role of oxidative stress is critical in the occurrence of sickle cell disease. The study has analyzed different groups of patients considering the Homozygous (SS), Heterozygous (AS) and Iron Deficiency Anemia (IDA). The findings of the observation have suggested that the muted Hb leads to profound changes in red blood cells metabolism and psychology. The reactive oxidants are playing a significant role in the makers of tissues and increase the disease severalty. The major findings of this study suggested that oxidative stress is an important hallmark of SCD that leads to damage of several organs[9]. An improved understanding of oxidative stress will lead to targeted antioxidants therapy that helps to prevent or delay the development of organs and increase the complications in the patient. Blood viscosity and erythrocyte deformability are the main determinants that maintain microcirculation. The changes in the level of Hb is increasing the causes for high blood pressure and increasing fatigue among the people. Apart from this, Chirico et al., (2016) have highlighted the issues related to blood viscosity and decrease in RBC deformability. The oxidative stress is determined through the radical scavengers and also iron chelators on sickle cell and their membrane. The lacking of Vit C and E is increasing the chance of sickle cell in individuals as well as the super oxidants are also playing a significant role. The study has analyzed the transfusion dependents for diagnosing the sickle cell and found that people with higher super oxidants are having higher chances of getting affected by the SCA[10]. The mutation in RNA and heterozygosis is influencing the health conditions of an individual. The major findings of the study involve the non-transfusion dependents and transfusion of the internal acid required for the body. The study has highlighted the areas of concern related to the severity of clinical symptoms and complications. The lipid profile of the SCA patients was compared and it was found that the changes in the body functions of the patients were affecting the organ activities and influencing the approach of the individual. The blood flow rate is higher among the

normal people but the SCA patients were having the low determinates of blood viscosities at shear rate[11].

In addition to this, the study has proposed different trends for managing the issues[12]. The imperative trends for offering the treatment is involving the improvement in the education and providing the information related to the sexual orientation. The interracial marriage and changes in the genetic codes of the individual is having a significant impact on the possibility of sickle cell disease. However, the changes in the health care services and professional approach for maintaining the prevention and regular research and intervention related to the impact of sickle cell can be useful for minimizing the impact of the issues. The cost of the treatment is higher and having a direct association with the approach of the individual to get the required treatment. The children who have sickle cell disorder by birth have issues related to the lungs, liver and spleen. The prior diagnose of issues can help manage the health and offer clinical care to cure the patient. The differences in the level of mean corpuscular volume and mean platelets volume is playing a significant impact in the health of an individual. The differences in MCH value and blockage in the blood cells is increasing the problem related to the sickle cell. The oxidative stress is an imbalanced redox status which is causing due to overproduction of the oxidants and depletion of antioxidant. This kind of situation is creating the issue in the blood flow of the individual and leading towards the disease related to pain episode and stroke. Different studies on related aspects of oxidative stress [12,13] and sickle cell disease were reported[14-17].

According to the views of Chirico et al., (2016), the denatured hemoglobin releases iron which may produce free radical through fentone reaction. These free radicals target the erythrocyte membrane by initiating lipid pre-oxidants which may involve in the progressions of sickle cell. The free radicals are playing a significant role in the improvement of the tissues and breakdown of the radical species. The oxidants are providing the proper support for the neutralization of the stress making factors but improvement in the oxidants is affecting the flow of the blood and increasing the issues related to organ damage and pain in the different parts of the body. The balance in the oxidants and antioxidants is playing an important role in the accumulation of ROS within body and the process is known as oxidative stress making. The improvement in the oxidative stress is leading towards the cancer. However, the human body is having inherent mechanism for protecting against free radical and other ROS that called as antioxidants stress. In the current scenario, the medical professionals are analyzing the level of free radicals and identifying the impact of the oxidants which help to provide the better treatment options. Moreover, the changes in the level of Vitamin E and C are also having direct impact on the health of an individual. To avoid the issues related to the sickle cell and oxidative stress bio makers, the regular diagnose till the age of 12 years is good or the parents can make use of screening of the newborn. The prior identification and monitoring can be helpful for minimizing the impact of the issues and support the medical professionals to provide better treatment.

REFERENCES:

1. Voskou, S., Aslan, M., Fanis, P., Phylactides, M. and Kleanthous, M., 2015. Oxidative stress in β-thalassaemia and sickle cell disease. Redox biology, *6*, pp.226-239.
2. Van Beers, E.J. and van Wijk, R., 2018. Oxidative stress in sickle cell disease; more than a DAMP squib. Clinical hemorheology and microcirculation, *68*(2-3), pp.239-250.

3. Biswal, S., Rizwan, H., Pal, S., Sabnam, S., Parida, P. and Pal, A., 2019. Oxidative stress, antioxidant capacity, biomolecule damage, and inflammation symptoms of sickle cell disease in children. Haematology, *24*(1), pp.1-9.
4. Belcher, J.D., Chen, C., Nguyen, J., Zhang, P., Abdulla, F., Nguyen, P., Killeen, T., Xu, P., O'Sullivan, G., Nath, K.A. and Vercellotti, G.M., 2017. Control of oxidative stress and inflammation in sickle cell disease with the Nrf2 activator dimethyl fumarate. Antioxidants & redox signaling, *26*(14), pp.748-762.
5. 5.Antwi-Boasiako, C., B Dankwah, G., Aryee, R., Hayfron-Benjamin, C., S Donkor, E. and D Campbell, A., 2019. Oxidative profile of patients with sickle cell disease. Medical Sciences, *7*(2), p.17.
6. Nader, E., Romana, M. and Connes, P., 2020. The red blood cell—inflammation vicious circle in sickle cell disease. Frontiers in immunology, 11, p.454.
7. Hermann, P.B., Pianovski, M.A.D., Henneberg, R., Nascimento, A.J. and Leonart, M.S.S., 2016. Erythrocyte oxidative stress markers in children with sickle cell disease. Jornal de pediatria, *92*, pp.394-399.
8. Niihara, Y., Miller, S.T., Kanter, J., Lanzkron, S., Smith, W.R., Hsu, L.L., Gordeuk, V.R., Viswanathan, K., Sarnaik, S., Osunkwo, I. and Guillaume, E., 2018. A phase 3 trial of l-glutamine in sickle cell disease. New England Journal of Medicine, *379*(3), pp.226-235.
9. Chirico, E.N., Faës, C., Connes, P., Canet-Soulas, E., Martin, C. and Pialoux, V., 2016. Role of exercise-induced oxidative stress in sickle cell trait and disease. Sports Medicine, *46*(5), pp.629-639.
10. Connes, P., Alexy, T., Detterich, J., Romana, M., Hardy-Dessources, M.D. and Ballas, S.K., 2016. The role of blood rheology in sickle cell disease. Blood reviews, *30*(2), pp.111-118.
11. Telen, M.J., Malik, P. and Vercellotti, G.M., 2019. Therapeutic strategies for sickle cell disease: towards a multi-agent approach. Nature reviews Drug discovery, *18*(2), pp.139-158.
12. Muley, P.P., Muley, P.A., 2020. Oxidative stress in seminal plasma and its relation to fertility potential of human male subjects. Journal of Datta Meghe Institute of Medical Sciences University 15, 172–175. https://doi.org/10.4103/jdmimsu.jdmimsu_110_20
13. Ambad, R.S., Jha, R.K., Bankar, N., Kalambe, M., Shrivastava, D., 2020c. Role of oxidative stress and antioxidant in preeclampsia: A study in rural population. International Journal of Research in Pharmaceutical Sciences 11, 3322–3328. https://doi.org/10.26452/ijrps.v11i3.2465
14. Baliga, S., Chaudhary, M., Bhat, S., Bhansali, P., Agrawal, A., Gundawar, S., 2018. Estimation of malondialdehyde levels in serum and saliva of children affected with sickle cell anemia. Journal of Indian Society of Pedodontics and Preventive Dentistry 36, 43–47. https://doi.org/10.4103/JISPPD.JISPPD_87_17
15. Chandak, P., Vagga, A., Chaudhary, G.A., 2019b. Haematological profile in patient of sickle cell anaemia in vidarbha region. International Journal of Pharmaceutical Research 11, 1161–1164. https://doi.org/10.31838/ijpr/2019.11.01.205
16. Ehtesham, M.A., Lakhkar, B., Adkane, R., 2020. Lactate dehydrogenase as predictor for severity in sickle cell disease. International Journal of Current Research and Review 12, 3–5. https://doi.org/10.31782/IJCRR.2020.SP84
17. Jadhav, U., Babu, R., Ghewade, B., Lanjewar, A., Gandhasiri, D., 2020a. Acute chest syndrome, a distinctive manifestation in sickle cell disease-A case study. Journal of Datta Meghe Institute

of Medical Sciences University 15, 492–494. https://doi.org/10.4103/jdmimsu.jdmimsu-166-20