Journal of Current Biomedical Research (2021)

The Use of Vitamin C for Prophylaxis and Management of COVID-19 in G6PD Deficiency; A Case Report in Nigeria.

Ohanube GAK[1], Ikeagwulonu RC[2], Obeta MU[3], Okoro SC[4]

1. Department of Biomedical Science, University of Applied Science, Bonn-Rhein-Sieg, https://orcid.org/0000-0003-1340-3223
2. Alex Ekwueme Federal University Teaching Hospital, Abakaliki-Nigeria. https://orcid.org/0000-0002-9455-5124
3. Medical Laboratory Management, Federal School of Medical Laboratory Science, Jos, Nigeria. https://orcid.org/0000-0002-1382-6034
4. Kano State Hospital Management Board, Gaya Zone 5, Kano State, Nigeria

Corresponding Author: Obeta MU, Department of Medical Laboratory Management, Federal School of Medical Laboratory Science, Jos, Nigeria uchejesoobeta@gmail.com

ABSTRACT

The rationale behind this case report is to identify some adverse effects, if any, in the use of vitamin C (ascorbic acid) by those living with Glucose-6-phosphate dehydrogenase (G6PD) deficiency, an enzymopathy affecting about 400 million people globally. The study was done to ascertain the prophylactic efficacy of ascorbic acid among Nigerians towards contacting COVID-19. There was a case of a G6PD deficient caregiver who agreed for the use of the information voluntarily provided based on his experience in the use of vitamin C between March 15, 2020, and October 30, 2020. The only time the subject had heartburn, it was quelled using vitamin C enriched fruits. The caregiver experience as a deficient patient of Glucose-6-phosphate dehydrogenase and the use of Vitamin C for COVID-19 prophylaxis without any serious contraindication shows that vitamin C is equally very good in the prophylaxis and management of COVID-19 in G6PD deficient subjects.

Keywords: COVID-19; Ascorbic acid, Garcinia kola, Glucose-6-phosphate dehydrogenase, Acute Haemolytic Anaemia.

INTRODUCTION

The prophylactic use of vitamin C during this pandemic has no doubts brought some relief to the world, especially Africans. For centuries, vitamin C continues to nourish and replenish stressed cells; strengthen immunity; serve as an antioxidant, promote wound healing, and rejuvenate the extracellular matrix. It slows the rate of progression of cancerous growth, reduces cardiovascular diseases, calm inflammation of varying degrees(Carr and Maggini, 2017, Chambial *et al*., 2013) even the inflammation which culminates into cytokine storm, multiple organ failure and death. All these attributes make it invaluable in controlling this pandemic. Experts have proposed the daily use of vitamin C (100mg-1000mg) for prophylaxis due to its acidic properties which aid the immunological and physiological roles it plays in humans; just like (1000mg-2000mg) was proposed for a strategic cure (Ohanube and Obeta, 2020; Ohanube, Obeta and Ikeagwulonu, 2020)

Discussing with Nigerians via social media platforms, all one could palpate is a group of happy people who vociferously chorus “Vitamin C is the game”. A close investigation on the reality on the ground would make any discerning mind agree with this most populous black nation whose

people have outlived myriads of viral diseases ranging from Lassa to Ebola and now coronavirus disease of 2019 (COVID-19) on her popular choice of vitamin C. They have all found strengths in their weaknesses. They embraced vitamin C based regimen to keep hopes alive, pending the arrival of a vaccine which is clinically proven to be safe.

It is now nine months since her index case of COVID-19, Nigerians just like other Africans are not dying *en masse* against famous prediction, despite the low testing capacity of most African countries (See table 1).

Countries	Estimated population	Cases	Number of deaths	Case fatality ratio	Deaths per million
Australia	26,000,000	27,686	907	3.276	35
Brazil	211,000,000	5,701,283	162,842	2.856	772
China	1,450,000,000	86,284	4,634	5.370	3
India	1,380,000,000	8,636,011	127,615	1.478	93
Nigeria	206,000,000	64,336	1,160	1.803	6
Russia	146,000,000	1,836,960	31,593	1.720	216
U.s. a	330,000,000	10,568,714	245,943	2.327	745

Table 1: A table showing the Case Fatality Ratio (CFR) and Deaths Per Million (DPM) of the different countries with the largest population in their continents. India and China were added, because aside China being the abode of the index case, India is next in demography(Worldometer, 2020).

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is a heritable metabolic abnormality caused by mutations in the G6PD gene linked to an X-chromosome. This condition leads to enzymopathy, a term used to describe the deficiency or inefficiency of enzymes, in this case, G6PD. The low levels of this G6PD enzyme culminate into the fragility and impaired function of the bearer's red blood cells heralding their premature lysis (breakage) which leads to haematuria (blood in urine); this accelerated loss of blood via the urine, predisposes one to acute haemolytic anaemia (AHA) due to the body's inability to compensate for it. This deficiency is typically induced by some precipitating factors such as infectious diseases, certain drugs, and eating fava beans in what is known as favism. In favism, symptoms such as fatigue, shortness of breath, rapid heartbeat, jaundice or yellow skin colour, dark urine and splenomegaly are presented. While post-therapeutic haematuria and favism are pathognomonic for this deficiency, diagnosis is confirmed via red cell enzyme activity assay. It is classified into five different classes depending on their respective severity and the absence or presence of causal factors; while the clinical implications are grouped into three variant forms, which are G6PD Mediterranean, G6PD A- and G6PD Mahidol. Some literature has shown that G6PD deficiency prevents severe malaria and that there is a strong correlation between the geographic distributions of the two. This distribution is seen in Africa, the Middle East, certain parts of the Mediterranean, and certain areas in Asia (Beutler, 2008; (Ruwende and Hill, 1998; Luzzatto, 2006). Other literature also notes that synthetic ascorbic acid is contraindicated in conditions like thalassemia, G6PD deficiency, sickle

cell disease, and hemochromatosis, because it may induce acute haemolytic anaemia[8].

This work aims to determine if the daily use of ascorbic acid for a minimum of six months is contraindicated for those predisposed to haemolytic anaemia due to gene, using a G6PD deficient person. It also evaluates the use of vitamin C among Nigerians during this pandemic as a prophylactic product for COVID-19 prevention.

CASE REPORT

A clinical scientist of 38 years in age, who hails from Nigeria shares his experience. His status for G6PD deficiency was discovered in a prominent tertiary health institution in Enugu State, Nigeria in 2010 after he experienced haemolytic anaemia as a result of the anti-malaria he took. He has been on a daily dose of Ascorbic acid tablets (480mg) since March 15, 2020 till the time of this report. The only complaint he gave was slight heartburn when he took it with painkillers. Till date, he has not developed symptoms such as pyrexia, myalgia, cough, dyspnoea, anosmia, and anorexia which is typical of COVID-19. About using vitamin C for COVID-19, he says: “vitamin C works, it prevents the contacting of COVID-19 and some viral disease, and has no deleterious effects like haemolytic anaemia”. About protective effects of G6PD deficiency in “Plasmodiasis”, he went further to say: “I do have malaria, even the severe ones, what people should say is that G6PD deficiency can prevent deaths from malaria but it would be difficult for those of us with this deficiency to agree to the fact that it prevents severe malaria”.

Management and Outcome

The only time he had heartburn, he said he was advised to take Paw-Paw, which is another rich source of vitamin C to soothe it. He noted that he uses Garcinia Kola (Bitter Kola) twice daily, each of the times he had respiratory tract infections.

DISCUSSION

The CFR of 1.8 (see table 1), presents Nigeria as a country with many deaths higher than that of Russia and India; it also shows that China, the index case has the highest number of deaths[9]. However, in reality, Nigeria is known to be having fewer deaths than India and Russia; while it is no longer news that China has the least number of deaths. This scenario indicates that though CFR could be used to determine death rates from diagnosed cases of a disease(WHO, 2020); it may not be the most appropriate tool during or after a pandemic, especially in an African setting due to some factors which include laboratory testing capacity, making the mortality rate or DPM a preferred index. However, the mortality rate, which is the number of deaths from a specific cause per 100,000 of the population of a state or a country may not apply to this situation until after a period of time, say a year(WHO,2020); this makes DPM, a more appropriate tool. DPM is the number of deaths triggered at any time by a pandemic's aetiology per 1,000,000 population of a country. DPM as an index gives leeway in monitoring the efficiency of the control measures implemented by countries during a pandemic. It also helps to verify the progress made in saving lives, despite its limitation of only providing an estimate.

Glucose-6-phosphate dehydrogenase (G6PD) deficiency patients may experience haemolytic crises due to exposure to oxidative agents or viral infections such as COVID-19 leading to the disease severity (Jamerson, Haryadi and Bohannon, 2020). An *ex vivo* study by Wu *et al*.(2008), has it that G6PD-deficient cells are more vulnerable to human coronavirus infection than those with G6PD normal cells. The health worker who is highly exposed to COVID-19 and have a sound knowledge of the deleterious effects of Quinoline containing anti-malaria drugs since 2010 in Enugu Nigeria, did not want to be infected with COVID-19 either does he want to use this Quinoline derivative for prophylaxis as suggested by some school of thought. Thus, for prophylaxis, he adopted a daily use of ascorbic acid tablets (480mg) as proposed by experts14. (Ohanube et al., 2020, Ohanube and Obeta, 2020). He also believes Garcinia Kola (Bitter kola), a fruit mostly seen in West Africa is a rich source of ascorbic acid, hence can be a wonderful substitute (Egbeahie, Idu and Chidi-Egboka 2018).

While Al-Abdi and Al-Aamri advise that people with G6PD deficiency who contracted COVID-19 be treated with caution when using chloroquine or hydroxychloroquine, which are classic examples of quinoline derivative (Al-Abdi and Al-Aamri, 2020); evidence abound suggesting that hydroxychloroquine has oxidative properties that could decrease glutathione levels and may cause severe haemolysis in G6PD-deficient patients. As such, the administration of hydroxychloroquine for prophylaxis or treatment of COVID-19 in G6PD deficiency could lead to worse prognosis associated with haemolytic crisis and COVID-19 severity (Jamerson, Haryadi and Bohannon, 2020; Frank, 2005; La Vieille, 2019); making vitamin C a choice in areas endemic for G6PD deficiency. Thus, the authors strongly advocate for the daily use of low-dose ascorbic acid (100mg-500mg) for prophylaxis and relatively high-dose (1000mg-2000mg) for symptomatic management even for G6PD deficient people[3,4], as they beg to differ on the opinion of Abdullah et al.[8], on the contraindication of Vitamin C in G6PD deficiency. This case was unique in the sense that most co-workers contacted COVID-19 during the case period but the case subject remained negative having commenced Vitamin C therapy early enough.

LESSONS LEARNT FROM NIGERIA

Ascorbic acid is not contraindicated in G6PD deficiency. G6PD deficiency does not preclude severe malaria.

CFR evaluates the testing capacity of nations; while DPM monitors the success of their control measures.

Garcinia kola could be an excellent alternative medicine to Ascorbic acid in preventing COVID-19.

CONCLUSION

Finally, this work has been able to provide evidence that ascorbic acid is not contraindicated in persons with G6PD deficiency. However, there is need for a

large-scale study using people with a known history of G6PD deficiency, Thalassaemia, Haemochromatosis and Sickle Cell Disease, to know if this is peculiar to only G6PD deficiency or if it applies to these other conditions.

The DPM of 6.0 presents Nigeria as one of the countries with the least number of deaths compared to her CFR of 1.8; this presents a better picture of the pandemic. Hence, it is safe to suggest that CFR be used to evaluate the testing capacity of countries and DPM be used to check the efficacy of the control measures.

The authors agreed that the Vitamin C played the prophylactic role on the G6PD deficient health worker considering the subject's inconsistence use of adequate protective materials at work and consistent use of vitamin C.

ACKNOWLEDGEMENT

Special thanks to the clinical scientist for granting us the consent to use his information.

AUTHOR'S CONTRIBUTION

Conceptualization, OGAK; Methodology, OGAK, OMU and OSC; Visualization, OGAK; Writing – Original Draft, OGAK, OMU, IRC, OSC; Writing – Review & Editing, OGAK, OMU.

DECLARATION OF INTEREST

The authors declare no competing interests.

REFERENCES

Abdullah M, Jamil RT, Attia FN. Vitamin C (ascorbic acid). InStatPearls [Internet] 2020 Feb 22. StatPearls Publishing.

Al-Abdi S. and Al-Aamri M. G6PD deficiency in the COVID-19 pandemic: "Ghost within Ghost" Hematol Oncol Stem Cell Ther,

Beutler E. Glucose-6-phosphate dehydrogenase deficiency: a historical perspective. Blood. 2008 January 1;111(1):16-24.

Carr AC, Maggini S. Vitamin C and immune function. Nutrients. 2017 Nov;9(11):1211.

Chambial, S., Dwivedi, S., Shukla, K. K., John, P. J., & Sharma, P. (2013). Vitamin C in disease prevention and cure: an overview. *Indian journal of clinical biochemistry: IJCB*, *28*(4), 314–328.

Egbeahie SE, Idu FK, Chidi-Egboka NC. Effect of Combined Intake of Garcinia Kola and Ascorbic Acid on Intraocular Pressure of Normotensive Nigerians. Journal of the Nigerian Optometric Association 2018;20(1):20-9.

Frank JE. Diagnosis and management of G6PD deficiency. Am Fam Physician 2005;72:1277e1282.

Jamerson BD, Haryadi TH, Bohannon A. Glucose-6-Phosphate Dehydrogenase Deficiency: An Actionable Risk Factor for Patients with COVID-19? Archives of Medical Research (2020)

La Vieille S, Lefebvre DE, Khalid AF, Decan MR, Godefroy S. Dietary restrictions for

people with glucose-6-phosphate dehydrogenase deficiency. Nutr Rev 2019; 77:96–106. https://doi.org/10.1093/nutrit/nuy053

Luzzatto L. Glucose 6-phosphate dehydrogenase deficiency: from genotype to phenotype. Haematologica/the hematology journal. 2006; 91(10)

Ohanube GAK, Obeta MU, Ikeagwulonu RC, and Jwanse IR. COVID-19: A Case Study of Using Vitamin C Enriched Plants and Ascorbic Acid as Cure. American Journal of Medical Case Reports, vol.8, no. 11 (2020): 435-437..

Ohanube GAK, Obeta MU. COVID-19: Novel Opinion on Strategic Prophylaxis and Cure Using Vitamin C (Ascorbic Acid). Acta Scientific Nutritional Health. (2020). 4(5): 32-33.

Ohanube GAK, Obeta UM, Ikeagwulonu CR. Case reports in the use of vitamin C based regimen in prophylaxis and management of COVID-19 among Nigerians. Journal of Current Biomedical Reports, 2020.1(2).

Ruwende CY, Hill A. Glucose-6-phosphate dehydrogenase deficiency and malaria. Journal of molecular medicine. 1998 June 1;76(8):581-8.

World Health Organization. Estimating mortality from COVID-19: scientific brief, August 4 2020. World Health Organization; 2020.

World Health Organization. Mortality rate (per 100 000 population). Retrieved November 12, 2020, from https://www.who.int/data/gho/indicator-metadata-registry/imr-details/3130

Worldometer. Countries where COVID-19 has spread. Retrieved November 11, 2020 from https://www.worldometers.info/coronavirus/countries-where-coronavirus-has-spread/

Wu Y-H, Tseng C-P, Cheng M-L, Ho H-Y, Shih S-R, Chiu DT-Y. Glucose-6-phosphate dehydrogenase deficiency enhances human coronavirus 229E infection. J Infect Dis 2008;197:812–6.