DETERMINING THE BURDEN AND CLINICAL SPECTRUM OF SEVERE MALARIA FROM ROUTINE HEALTH FACILITY BASED SURVEILLANCE AT APAC DISTRICT HOSPITAL: A CROSS-SECTIONAL STUDY.

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A RESEARCH DISSERTATION SUBMITTED TO BUSITEMA UNIVERSITY IN

PARTIALFULFILLMENTOF THEREQUIREMENT FOR THE AWARD

OF MASTER OFPUBLIC HEALTH DEGREE.

February, 2022

Declaration.

I **OCEN EMMANUEL** do declare that the work presented in this dissertation is a result of my original research work. Where I have used the works of other persons, due acknowledgements are clearly stated. No portion of this work has been submitted for the award of a degree or qualification to any other university or institute of higher learning.

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Acknowledgements

I would like to acknowledge the contribution of my supervisors. Firstly, Dr.Tegu Crispus who heavily invested in his time and knowledge to ensure this dissertation is completed. Secondly, Professor Peter Olupot-Olupot for his leadership in supervision, expertise on the subject matter, guidance and investing his time on this work.

Without these two supervisors, this work would probably not see the light of the day.

I also acknowledge the support from my classmates, especially Dr. Ronald Opito who has been a source of encouragement to me during my studies and research.

In a special way, I would like to thank all of my lecturers for the knowledge, skills and competences they imparted on me. They each encouraged me, especially Dr.Benon Wanume who went an extra mile to counsel me and support my studies. To All the lecturers, thank you so much. Your inputs into this research work were not in vain.

Dedication

This research work is dedicated to my beloved parents Muzee Ojede Benjamin (RIP) and Imat Joyce Akullu Ojede (RIP).

Acronyms

EIR   Entomological Infective Rate

GOU   Government of Uganda

HIV   Human Immune deficiency Virus

IPT   Intermittent Preventive Treatment in Pregnancies

IRS   Indoor Residual Spray

ITN   Insecticide Treated Nets

KAP   Knowledge, Attitude and Practice

LLINS   Long Lasting Insecticide Treated Nets

MOH   Ministry of Health

NGO   Non-Governmental Organization

P. falc.   *Plasmodium falciparum*

RDT   Rapid Diagnostic Test

UNICEF   United Nations International Children Fund

USD   United States Dollar

WHO   World Health Organization

Operational Definitions

Malaria: This is a mosquito-borne protozoal blood disease that is life-threatening and caused by any of the 5 human infecting *Plasmodium* parasites namely *Plasmodium falciparum*, *Plasmodium vivex*, *Plasmodium malariae*, *Plasmodium ovale* and *Plasmodium knowlesi*. It is transmitted through a bite of the female Anopheles mosquito from person to person. In Uganda almost all 99% of malaria infections are due to *Plasmodium falciparum* malaria[1].

Severe Malaria: This is defined as the presence of P.falciparum and one or more of the following signs, symptoms and laboratory tests, in the absence of an alternative cause; impaired consciousness, prostration, multiple convulsions, respiratory distress, shock, pulmonary oedema, hypoglycaemia, metabolic acidosis, anaemia, haemoglobinuria, hyperparasitemia or hyperlactatemia [2].

Clinical Presentation: It is defined as the typical signs and symptoms of malaria.

Clinical outcomes: The end result of admission and treatment of a child with severe malaria.

Normal Hospital Stay: Staying in the Hospital for 4 or less days after admission.

Prolonged Hospital Stay: Staying in the Hospital for more than 75th percentile of the median length of stay (more than 4 days) after admission.

Abstract.

Background: Most data describing severe malaria (SM) are from research settings, but these are driven by research funding. Routine facility-based data have therefore not been given priority to contribute to the descriptions of the burden and clinical spectrum of Severe Malaria. Exploring routine facility-based data is critical for contribution of data from non-research settings and for a complete picture of disease. Despite very high (>1,500) entomological inoculation rates (EIR) in Apac, there are no formal descriptions of severe malaria from the region. The aim of this study was to establish the burden and clinical spectrum of severe malaria from routinely collected facility-based surveillance data among children admitted at Apac District Hospital.

Materials and Methods: This was a cross sectional study taking the form of a secondary data review of the medical records of admissions in Apac District Hospital for the 24 months period of Jan 2019 to Dec 2020. I applied quantitative methodology of data collection and analysis. To determine the proportions of admissions resulting from severe malaria, all the 5631 records from the inpatient admission book was reviewed. Data abstraction of key variables was done on 745 files of admitted children who met the eligibility criteria using a customized proforma. The clean data were captured on excel database, exported to STATA version 14.0 statistical Package for further management and analysis. Univariate analyses included description of summary statistics including median age, proportions and frequencies, while Fisher's exact test was used to determine the associations with risk of death and clinical presentations of severe malaria. Multivariate analyses were done using multiple logistic regression to determine factors associated with prolonged Hospital stay.

Results: The data routinely collected in Apac District Hospital had varying levels of completeness as follows; Age 100% (n=5631), sex 99.3% (n=5589), date of admission 99.1% (n=5583), date of discharge 40.6% (n=2281) and outcome status 56.5% (n=3180). Severe malaria was the common reason for admission in Apac District Hospital, contributing to 64.8% (n=3649) of the 5631 total admissions,

followed by Pneumonia at 12.1% (n=681). The most common clinical presentations among these children with severe malaria in Apac District Hospital included; Fever 722 (97.3%), Cough 478 (64.2%), Vomiting 265 (38.7%), Diarrhea 192 (28.1%) and difficulty in breathing 122 (17.9%). The median length of hospital stay was 2(IQR; 2-4) days and 133 (17.9%) of the study participants stayed in the Hospital for more than 4 days (Prolonged stay). Majority of admitted children, 735 (98.7%) were Survivors while 10 (1.3%) died of malaria. At multivariate level, factors that were significantly associated with prolonged Hospital stay were, presenting with difficulty in breathing, aOR 1.83 (95%CI: 1.02-3.27, P=0.042) and Prostration aOR 8.47 (95%CI: 1.94-36.99, P=0.004).

Conclusion: Malaria is the major cause of Hospital admission in Apac District Hospital. There is low death rate resulting from malaria admissions in Apac District Hospital. Prolonged Hospital stay was associated with prostration and difficulty in breathing.

Recommendations: Patients presenting with difficulty in breathing and prostration need to be started on early treatment so as to reduce the length of Hospital stay.

Apac District Hospital needs to improve on the quality of malaria data collected so as to improve its usability for surveillance purposes.

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CHAPTER 1: BACKGROUND

Introduction

This chapter presents the background information, problem statement, study objectives and the justification of the study. It also presents the research questions and the conceptual framework. Finally, it outlines the chapters that are included in this dissertation.

Background

Globally, morbidity due to *Plasmodium falciparum* malaria accounts for 300-500 million clinical episodes, with 780,000 direct and 3 million indirect deaths annually [3,4] reported. There were an estimated 229million malaria cases in 2019 in 87 malaria endemic countries, declining from 238million in 2000. At the Global technical strategy for malaria 2016–2030 (GTS) baseline of 2015, there were 218million estimated malaria cases. The World Health Organization (WHO) African Region, with an estimated 215million cases in 2019, accounted for about 94% of cases. The analysis suggested that malaria mortality in sub-Saharan Africa was likely to double by the end of 2020[5].

Severe malaria is a life-threatening disease almost exclusive to Plasmodium falciparum malaria. An estimated 2 billion people live in areas with malaria, but about 230million cases occur every year [6]. Malaria is transmitted through the bites of an infected female anopheles mosquito. There are many Plasmodium species, but the five known to infect man include *Plasmodium falciparum*, *Plasmodium vivax*,

REFERENCES:

[1]. Yeka A, Gasasira A, Mpimbaza A, Achan J, Nankabirwa J, Nsobya S, et al. Malaria in Uganda: Challenges to control on the long road to elimination. I. Epidemiology and current control efforts. Acta Trop. 2012;121(3):184–95.

[2]. Kochar DK, Tanwar GS, Khatri PC, Kochar SK, Sengar GS. Clinical Features of Children Hospitalized with Malaria — A Study from Bikaner , Northwest India. 2010;83(5):981–9.

[3]. Olupot-Olupot P1 MK. Management of severe malaria: results from recent trials. 2013. 241–50 p.

[4]. Attaran A, Barnes KI, Curtis C, Alessandro U, Fanello CI, Galinski MR, et al. Viewpoint WHO , the Global Fund , and medical malpractice in malaria treatment. 2010;363:237–40.

[5]. WHO. World malaria report 2020: 20 years of global progress and challenges. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO. [Internet]. Vol. 73, Who. 2020. 1–4 p. Available from: https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2020

[6]. Murray CJ1, Rosenfeld LC, Lim SS, Andrews KG, Foreman KJ, Haring D, Fullman N, Naghavi M, Lozano R LA. Global malaria mortality between 1980 and 2010: a systematic analysis. Lancet. 2012;379((9814)):413–31.

[7]. WHO. Guidelines for the treatment of Malaria. Third Edit. Geneva: WHO; 2015.

[8].   WHO. WHO global malaria programme. World malaria report 2014. 2014.

[9].   Ricci F. Social Implications of Malaria a and Their Relationships with ith Poverty. 2012;

[10].   Silva LS, Silva-filho JL, Caruso-neves C. New Concepts in Malaria Pathogenesis : The Role of the Renin-Angiotensin System. 2016;5(January):5– 10.

[11].   CDC. Global Health Security: Top 10 Causes of Death. 2018.

[12].   WHO. Guidelines for the treatment of malaria. 2010.

[13].   Mpimbaza A, Walemwa R, Kapisi J, Sserwanga A, Namuganga JF, Kisambira Y, et al. The age-specific incidence of hospitalized paediatric malaria in Uganda. BMC Infect Dis. 2020;20(1):1–12.

[14].   Ohrt C, Roberts KW, Sturrock HJW, Wegbreit J, Lee BY, Gosling RD. Information systems to support surveillance for malaria elimination. Am J Trop Med Hyg. 2015;93(1):145–52.

[15].   Al-taiar A, Jaffar S, Assabri A, Al-habori M, Azazy A, Al-mahdi N, et al. Severe malaria in children in Yemen : two site observational study. :1–5.

[16].   Cserti-gazdewich CM, Dhabangi A, Musoke C, Ssewanyana I, Ddungu H, Nakiboneka-ssenabulya D, et al. Inter-Relationships of Cardinal Features and Outcomes of Symptomatic Pediatric Plasmodium falciparum Malaria in 1 , 933 Children in Kampala , Uganda. 2013;88(October 2007):747–56.

[17].   Kwenti TE, Nkume FA, Tanjeko AT, Kwenti TDB. The Effect of Intestinal Parasitic

Infection on the Clinical Outcome of Malaria in Coinfected Children in Cameroon. 2016;1–15.

[18]. Mockenhaupt FP1, Ehrhardt S, Burkhardt J, Bosomtwe SY, Laryea S, Anemana SD, Otchwemah RN, Cramer JP, Dietz E, Gellert S BU. Manifestation and outcome of severe malaria in children in northern Ghana. Am J Trop Med Hyg. 71(2):167–72.

[19]. Seidlein L Von, Olaosebikan R, Hendriksen ICE, Lee SJ, Adedoyin OT, Agbenyega T, et al. Predicting the Clinical Outcome of Severe Falciparum Malaria in African Children : Findings From a Large Randomized Trial. 2012;54.

[20]. Achidi EA, Apinjoh TO, Anchang-kimbi JK, Mugri RN, Ngwai AN, Yafi CN. Severe and uncomplicated falciparum malaria in children from three regions and three ethnic groups in Cameroon : prospective study. 2012;1–12.

[21]. Chiabi A, Takou V, Um SN, Essoh L, Immumboeh P. Initial treatment of severe malaria in children is inadequate – a study from a referral hospital in Cameroon. 2009;3(1):9–11.

[22]. Lacerda MVG, Mourão MPG, Alexandre MAA, Siqueira AM, Magalhães BML, Martinez-espinosa FE, et al. Understanding the clinical spectrum of complicated Plasmodium vivax malaria : a systematic review on the contributions of the Brazilian literature. 2012;1–18.

[23]. Hay SI, Okiro EA, Gething PW, Patil AP, Tatem AJ, Carlos A, et al. Estimating the Global Clinical Burden of Plasmodium falciparum Malaria in 2007. 2010;7(6).

[24]. Idro R, Aloyo J. Manifestations , Quality of Emergency Care and Outcome of Severe Malaria in Mulago Hospital , Uganda. :50–7.

[25]. Lee SY, Lee S, Tan JHH, Foo HSL, Phan PH, Kow AWC, et al. Factors associated with prolonged length of stay for elective hepatobiliary and neurosurgery patients : a retrospective medical record review. 2018;1–9.

[26]. Marfil-GarzaID BA, 1, Pablo F. Belaunzara´n-ZamudioID 2 AG-H, ZuñigaID AC, 2, Yanink Caro-Vega2 DK-S, Jose´ Sifuentes-Osornio1 2*. Risk factors associated with prolonged hospital length-of-stay : 18-year retrospective study of hospitalizations in a tertiary healthcare center in Mexico. 2018;4–17.

[27]. Vyas S, Bhatt G, Gupta K TH. A study of presentation and complications among the malaria death cases from three municipal corporation hospitals and civil hospital of Ahmedabad during the year 2007. Ann Trop Med Public Heal. 2011;4:81–5.

[28]. A.P.Velip, M.S.Kulkarni, D.D.Motghare FSV. Determinants of Hospital Stay among Malaria Patients at a Tertiary Care Hospital in Goa. 2006;38(1):115–7.

[29]. Sagbo GG, Alihonou F, Alao MJ, Tohodjèdé Y, Zohoun L, Bognon G, et al. The Determinants of Fatal Outcomes during Severe Malaria in Children at the HKM University Teaching Hospital of Cotonou-Benin. 2017;245–53.

[30]. Sikora SA, Poespoprodjo JR, Kenangalem E, Lampah DA, Sugiarto P, Laksono IS, et al. Intravenous artesunate plus oral dihydroartemisinin – piperaquine or intravenous quinine plus oral quinine for optimum treatment of severe malaria : lesson learnt from a field hospital in Timika , Papua , Indonesia. Malar J. 2019;1–

12.

[31]. Uganda Bureau of Statistics. National Population and Housing Census 2014 Area Specific Profiles Apac District. 2017;(April).

[32]. Kapesa A, Kweka EJ, Atieli H, Afrane YA, Kamugisha E, Lee MC, et al. The current malaria morbidity and mortality in different transmission settings in western Kenya. PLoS One. 2018;13(8).

[33]. Ravishankar MS, Mohan ME, Ramesh TP* DG. Spectral presentation of Plasmodium falciparum malaria in rural Karnataka. 2015;26(3):561–6.

[34]. Okello PE, Van Bortel W, Byaruhanga AM, Correwyn A, Roelants P, Talisuna A, et al. Variation in malaria transmission intensity in seven sites throughout Uganda. Am J Trop Med Hyg. 2006;75(2):219–25.

[35]. Ajetunmobi WA, Orimadegun AE, Brown BJ, Afolabi NK, Olabiyi FA, Anetor JI, et al. Haemoglobinuria among children with severe malaria attending tertiary care in Ibadan , Nigeria. 2012;1–8.

[36]. Augustin Mulangu Mutombo1, Olivier Mukuku2,&, Kristel Nzeba Tshibanda2, Edouard Kawawa Swana3, Eric Mukomena3, Dieudonné Tshikwej Ngwej1, Oscar Numbi Luboya1, 2, 3, Jean-Baptiste Kakoma4, Stanislas Okitotsho Wembonyama1, Jean-Pierre Van Geertruyden5 PL, 1Département. Severe malaria and death risk factors among children under 5 years at Jason Sendwe Hospital in Democratic Republic of Congo. 2018;8688:1–8.