RANZCOG WOMEN'S HEALTH FOUNDATION RESEARCH SCHOLARSHIP/FELLOWSHIP

PROGRESS REPORT

Scholarship/Fellowship: Norman Beischer Clinical Research Scholarship 2020-2021

Recipient: Manarangi De Silva

Project Title: Improving maternal health in the Asia-Pacific region

Synopsis

Maternal health outcomes in the Asia-Pacific region are poor and an area of great unmet need. During my PhD I propose to improve these outcomes by conducting research investigating maternal mortality and morbidity in the Asia-Pacific, specifically in the Solomon Islands, and investigating the potential role of antenatal betel nut consumption in contributing to adverse pregnancy outcomes. This project will determine ways to improve and reduce adverse maternal outcomes in the Asia-Pacific region.

Background

<u>The Asia-Pacific region</u>: Maternal outcomes remain poor in low and middle-income countries (LMICs), particularly in the Asia-Pacific. The cultural diversity, geographical isolation, poverty and poor health systems all contribute to the *lack* of improvement of these outcomes over the last decade (1,2).

<u>The Solomon Islands</u>: The Solomon Islands is a LMIC in the Pacific region with a population of approximately 600,000 spread across an archipelago of over 990 islands. Like many other Pacific islands, the country continues to face significant geographical, economic, cultural and logistical barriers which impact the availability and quality of obstetric care and research capacity. This has resulted in *very little reliable data on maternal and neonatal outcomes in the Solomon Islands*. The National Referral Hospital (NRH) of Solomon Islands, located in the nation's capital of Honiara, is the only tertiary hospital in the country and has approximately 5000-6000 deliveries per year.

Maternal mortality and morbidity in the Solomon Islands: Progress in the reduction of maternal mortality has been slow with the global maternal mortality rate (MMR) remaining high, at 216 per 100,000 live births (1). Over the last 20 years, there has also been increased focus on severe maternal morbidity (2, 4) with 10 million women presenting with life threatening complications related to pregnancy each year, globally. The current official MMR of 114 deaths per 100,000 live births ranks the Solomon Islands 113th out of 216 globally (1). We recently completed a review of all maternal mortality at NRH between 2013-2017, which revealed 39 maternal deaths. Alarmingly, this places the maternal mortality rate of the hospital (139/100,000) above that of the national rate (114/100,000). Overall, 79% of deaths were deemed preventable. These findings highlight the urgent need for further investigation to improve maternal morbidity and mortality in the Solomon Islands.

Betel nut, the fourth most abused substance globally: Betel nut, also known as areca nut, is extremely common in many LMICs, especially amongst Asian, African and Pacific Island populations (5, 6, 11). It is highly addictive and the main active ingredient, arecoline, has been well-described for its carcinogenic effects on the oral mucosa (2). It has been found to increase both parasympathetic and sympathetic activity, resulting in hypertension, increased risk of arrhythmias and bronchospasm (6, 7, 12). In many countries, it is consumed with other substances, such as tobacco. Solomon Islands is unique in that betel nut is often chewed in isolation, making it an ideal site for investigation of its effects in the absence of confounders. Importantly, betel nut may also play a role in maternal and neonatal morbidity. Recently, we undertook the first systematic review and meta-analysis investigating the association between betel nut use during pregnancy and the risk of adverse perinatal outcomes. Our review revealed only 8 eligible studies, all based in the Asia-Pacific and found a significant association between low birth weight and betel nut exposure. However, the studies had little information regarding hypertensive disorders of pregnancy and were of varying quality. This highlights the need for further, larger and more focussed prospective studies investigating the effect of antenatal betel nut consumption and whether this may be a modifiable risk factor for hypertensive disorders of pregnancy and other adverse maternal and neonatal outcomes.

Objectives

Overall Aim: To investigate preventable factors which contribute to maternal morbidity and mortality in the Asia-Pacific, specifically in the Solomon Islands, in order to identify potential areas for advancement that will improve maternal and neonatal outcomes in the region.

Aim 1: To investigate the incidence, risk factors and management of maternal morbidity/near miss and mortality in the Solomon Islands over 24 months.

Aim 2: To investigate the role of betel nut consumption as a risk factor for hypertensive disorders of pregnancy in a case-control study recruiting 250 participants per group (total = 500 participants).

Aim 3: to investigate the role of betel nut consumption as a risk factor for a range of major adverse pregnancy outcomes in a large, prospective cohort study over 18 months.

Progress/Update

Due to COVID-19, all data collection for our projects was halted in March 2020 by the Ministry of Health, Solomon Islands, and is yet to resume. We have requested permission to resume research activities and are awaiting confirmation with expectation of commencement in March 2021.

Part 1: Data collection has commenced in June 2019 – Feb 2020. We expect to restart data collection in March 2021 if permitted, and this project will be completed in August 2022.

Part 2: We have conducted a systematic review and meta-analysis investigating the association between betel nut and adverse pregnancy outcomes, identifying only 8 studies, highlighting the need for further research. Recruitment began in late May 2019, with all controls collected. An additional 45 cases are needed to reach the required sample size. We expect another 4-6 months of data collection will enable completion of this project in 2021.

Part 3: Ethical approval was granted for this study in 2019 (#HREA006/20). Commencement was scheduled to commence in March 2020; however, this project has not commenced due to the halting of all research in the Solomon Islands from March 2020. We expect to commence this project in May 2021, if permitted, and collect data until October 2022.

Conclusions

The pausing of research due to the global COVID-19 pandemic has significantly affected progress of our 3 research projects. However, we are optimistic that we will be permitted to recommence these projects in 2021.

Budget				
2020 PhD Scholarship salary	30,0000			
2021 PhD Scholarship salary	30,0000			
References				

- 1. Kassebaum NJ, Barber RM, Bhutta ZA, Dandona L, Gething PW, Hay SI, et al. Global, regional, and national levels of maternal mortality, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. The Lancet. 2016;388(10053):1775-812.
- 2. Geller SE, Koch AR, Garland CE, MacDonald EJ, Storey F, Lawton B. A global view of severe maternal morbidity: moving beyond maternal mortality. Reprod Health. 2018;15(Suppl 1):98.
- 3. Callister LC, Edwards JE. Sustainable Development Goals and the Ongoing Process of Reducing Maternal Mortality. J Obstet Gynecol Neonatal Nurs. 2017;46(3):e56-e64.
- 4. Tunçalp Ö, Hindin MJ, Souza JP, Chou D, Say L. The prevalence of maternal near miss: a systematic review. BJOG: An International Journal of Obstetrics & Gynaecology. 2012;119(6):653-61.
- 5. Berger KE, Masterson J, Mascardo J, Grapa J, Appanaitis I, Temengil E, et al. The Effects of Chewing Betel Nut with Tobacco and Pre-pregnancy Obesity on Adverse Birth Outcomes Among Palauan Women. Matern Child Health J. 2016;20(8):1696-703.
- 6. Senn M, Baiwog F, Winmai J, Mueller I, Rogerson S, Senn N. Betel nut chewing during pregnancy, Madang province, Papua New Guinea. Drug Alcohol Depend. 2009;105(1-2):126-31.
- 7. Javed F, Bello Correra FO, Chotai M, Tappuni AR, Almas K. Systemic conditions associated with areca nut usage: a literature review. Scandinavian Journal of Public Health. 2010;38(8):838-44.
- 8. Shih YT, Chen PS, Wu CH, Tseng YT, Wu YC, Lo YC. Arecoline, a major alkaloid of the areca nut, causes neurotoxicity through enhancement of oxidative stress and suppression of the antioxidant protective system. Free Radical Biology & Medicine. 2010;49(10):1471-9.
- 9. Mol BWJ, Roberts CT, Thangaratinam S, Magee LA, de Groot CJM, Hofmeyr GJ. Pre-eclampsia. The Lancet. 2016;387(10022):999-1011.
- 10. Sibai B, Dekker G, Kupferminc M. Pre-eclampsia. The Lancet. 2005;365(9461):785-99.
- 11. de Costa C, Griew AR. Effects of betel chewing on pregnancy outcome. Australian & New Zealand Journal of Obstetrics & Gynaecology. 1982;22(1):22-4.
- 12. Al-Rmalli SW, Jenkins RO, Haris PI. Betel quid chewing elevates human exposure to arsenic, cadmium and lead. J Hazard Mater. 2011;190(1-3):69-74.