MAGNITUDE AND TYPE OF MATERNAL BACTERIAL COLONISATION AT DELIVERY AND RISK OF EARLY-ONSET NEONATAL SEPSIS OF THEIR BABIES ADMITTED TO NEONATAL INTENSIVE CARE UNIT AT UNIVERSITY TEACHING HOSPITAL, LUSAKA, ZAMBIA

BY

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Dissertation submitted to the University of Zambia in partial fulfilment of the requirements for the award of degree of Master of Medicine in Obstetrics and Gynaecology

The University of Zambia

Lusaka

2019

DECLARATION

I declare that this dissertation is my original work and has never been presented or submitted anywhere for the award of any degree before. I therefore present it for the award of the degree of Master of Medicine in Obstetrics and Gynaecology of The University of Zambia, Lusaka, Zambia.

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APPROVAL

The dissertation of **Dr. Whyson Thaulo Munga** is approved as fulfilling part of the requirements for the reward of the degree of **Master of Medicine in Obstetrics and Gynaecology** by the University of Zambia.

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ABSTRACT

The incidence of early neonatal deaths and infections varies worldwide depending on the quality of antenatal care, intrapartum services and neonatal intensive care unit services. It is estimated that ninety eight percent of newborn deaths due to infections occur in developing countries mostly in Africa and Asia while two percent occur in developed countries. According to the Perinatal Audit Reports for the University Teaching Hospital, Neonatal Intensive Care Unit (UTH, NICU) in 2015, sixty percent of the admissions resulted in neonatal deaths within seven days of life. There were several different causes attributed to these deaths, but fifty percent were due to neonatal infections. Of these almost two-thirds (62.4%) were due to early onset sepsis. This study aimed at exploring the maternal bacterial colonisation of the vagina and perineum of the women in labour at UTH and whether it resulted in early infections in their newborn babies admitted to NICU.

This was a prospective cross-sectional study of women that delivered a singleton baby by vaginal delivery whose newborns were admitted to NICU for any reason. After consent, a structured interviewer administered questionnaire was used to collect the demographic, reproductive, medical, perinatal and social characteristics of the women. Vaginal and rectal swabs (to represent perineum) were taken from the eligible mothers in the immediate postpartum period and sent to the UTH laboratory for microscopy, culture and sensitivity. Similarly, blood cultures from the eligible newborns, as was standard of care, were also collected before administration of any antibiotics at admission to NICU. The descriptive data of the maternal and newborn characteristics and their culture results were presented in summary form.

Ninety-four mother-newborn dyads were enrolled. Of these, 87 (92.6%) of the vaginal swabs had normal flora on culture. A further 7 (7.4%) had Escherichia coli, Morganella morganii, Staphylococcus species and Staphylococcus epidermidis isolated. Also, 92 (97.9%) of the rectal swabs had normal flora isolations and 2 (2.1%) with Salmonella species isolated. There were no beta haemolytic Streptococcus in either swabs. The newborns blood culture results showed 93 (98.9%) with no growth and no isolations and 1(1.1%) with Staphylococcus epidermidis isolated attributed to possible contamination.

This study population showed women in labour could not be the likely source of the high levels of infections in the newborns as previously suspected. The conclusion from this study was that maternal colonisation of the vagina and rectum in the study population showed no Group B streptococcus but a predominance of normal flora. There were no isolations in the blood cultures taken at admission from the newborns in NICU and hence it was not possible to link maternal colonisation with early newborn infections of babies admitted to NICU in this series. Studies with larger numbers are needed to better understand the source of early newborn infections. Continued surveillance and infection prevention measure are recommended.

Key words: newborns, early neonatal infections, bacteraemia, and bacterial meningitis.

DEDICATION

I dedicate this dissertation to my dear wife, Nyamazao Mtonga Munga, our lovely children, Peter, Jesse and Wezi, my mother, Tisayine Phiri Munga, my father, Whyson Munga (Late) and above all God to whom I owe the purpose for my existence.

ACKNOWLEDGEMENTS

This work has been a culmination of invaluable contributions of many persons who played different roles in the study. Appreciation go to; the consultants, fellow postgraduate doctors, midwives, resident medical officers in the neonatal intensive care unit, the critical care nurses and the biomedical scientists all of the University Teaching Hospital, Lusaka, Zambia.

With a deep sense of appreciation, I would like to pay special acknowledgements to the following people:

1. My supervisor and Head of Training, Department of Obstetrics and Gynaecology, Prof. Bellington Vwalika, Mr Yusuf Ahmed, Consultant Obstetrician and Gynaecologist for their advice, guidance, encouragement, prompt responses and support.
2. Dr Samson Chisele, Consultant Obstetrician and Gynaecologist and Dr Wilbroad Mutale, Lecturer, Consultant Public Health Specialist for their advice and support.
3. Dr Sylvia Machona, Consultant Paediatrician, Mrs Jean Musonda, Critical Care Nurse and Miss Kutemba Lyangenda, Registered Midwife for the human resource and logistical mobilisation and coordination of sample collection.
4. Mr Mox Kalumbi Malama, Head of Microbiology Laboratory and Mrs Leocrisia Mwanamoonga Chitimbwa, Biomedical Scientist for human resource and laboratory logistical mobilisation and for the coordination and management of laboratory sample analysis and results management.
5. Mr Johnny Banda, Statistician for his input in data analysis and mentorship.
6. All the women together with their newborns who took part in the study.

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ABBREVIATIONS

BMC	Biomed Central
cART	Combination Antiretroviral Therapy
CI	Confidence Interval
GA	Gestation Age
GBS	Group B Streptococcus
GPPF	Graduate Proposal Presentation Forum
GRZ	Government of the Republic of Zambia
HIV	Human Immunodeficiency Virus
NICU	Neonatal Intensive Care Unit
PCR	Polymerase Chain Reaction
PG	Postgraduate
SPSS	Statistical Package for Social Sciences
PPROM	Preterm Pre-labour Rupture of Membranes
PROM	Pre-Labour Rupture of Membranes
UNZA	University of Zambia
UNZABREC	University of Zambia Biomedical Research Ethics Committee
UTH	University Teaching Hospital
WHO	World Health Organization

CHAPTER ONE: INTRODUCTION

1.1 Background

It is estimated that ninety eight percent of newborn deaths due to infections occur in developing countries mostly in Africa and Asia while two percent occur in developed countries (WHO, 1999).

The incidence of early neonatal deaths and infections varies worldwide depending on the quality of antenatal care, intrapartum services and neonatal intensive care unit (NICU) services (Nelsons, 2013). Early onset neonatal infections have been defined based on the age of onset, with bacteraemia and bacterial meningitis mostly occurring in the first 72 hours of life in hospitalised infants in NICU and less than 7 days of life in non-hospitalised infants (Nelsons, 2013). Late onset neonatal sepsis on the other hand occur after 72 hours of life in hospitalised infants in NICU and more than 7 days of life in non-hospitalised infants and may be caused by vertically or horizontally acquired pathogens (Nelsons, 2013).

A study done in coastal Kenya gave a twelve percent prevalence of Group B Streptococcal (GBS) maternal colonisation with a comparatively high incidence of associated stillbirths and early onset neonatal disease in the hospital of up to 23 per 1000 live births (Seal et al, 2016). There were no research publications from other regions and from Zambia (local) that were specific on the correlation of early neonatal infections with those in their mothers.

Sixty percent of the total admissions at the University Teaching Hospital (UTH) Neonatal Intensive Care Unit (NICU) in the year 2015 resulted in neonatal deaths within seven days of life (2015, UTH, NICU, Perinatal Reports). There were several different causes attributed to these deaths, but fifty percent were due to neonatal infections. Of these almost two-thirds (62.4%) were due to early onset sepsis. The causative organisms of neonatal sepsis that were being isolated in blood cultures from the hospitalised infants in the NICU at the UTH were varied from bacterial, fungal and viral. The commonest isolated organisms were Group B Streptococci (GBS) and Escherichia coli and unusually common organisms such as Klebsiella. These unusual organisms were very difficult to treat as they were only responding to very expensive

and usually unavailable antibiotics. This posed a challenge in the treatment options that could be available then and in the future

There was very little information as to what the sources of those infections in NICU were and maternal carriage of organisms was suspected to be one cause. This research, therefore investigated the extent of colonisation of organisms in mothers' reproductive tracts and the rectums and whether this resulted in organisms in the blood cultures from the hospitalised newborns in NICU at the UTH.

1.2 Statement of the Problem

Early infections in newborns admitted in the NICU at the UTH were on the increase with a prevalence of 62.4%, and causing substantial mortality and morbidity (Perinatal Audit Reports for UTH, NICU, 2015). Despite empirical treatment of all the newborns admitted to NICU with parenteral antibiotics, the outcome still remained very poor. This situation was further compounded by the emergence of resistant strains of bacteria e.g. Klebsiella to the commonly used parenteral antibiotics. Previous efforts to identify the source of these infections had included swabbing of delivery beds, resuscitaires and the floors from the UTH labour ward and theatres annually to ascertain if there were bacterial colonisations. The results were unrevealing. The positive blood culture results from samples collected from the newborns as early as 0-24 hours of admission to NICU raised suspicion for possible vertical transmission of these bacterial infections. This study aimed at investigating the microbial colonisation in the reproductive tracts and perineums of mothers in labour at UTH and whether it resulted in microbial infections in their respective newborns admitted to NICU. There were no previous studies of this nature done in Zambia and Africa. This study was therefore necessary not only to fill in the information gap but also to form a basis for future evidence based practice.

1.3 Research Question

Does maternal bacterial colonisation of the vagina and perineum of women in labour at UTH result in early infections in newborn babies admitted to NICU?

1.4 Objectives

1.4.1 General Objective

To explore the maternal bacterial colonisation of the vagina and perineum of women in labour at UTH and whether it results in early infections in newborn babies admitted to NICU

1.4.2 Specific Objectives

i. To identify the microorganisms colonising the vagina and perineum of mothers in labour at UTH
ii. To identify any microorganisms cultured in blood of the newborn babies delivered vaginally at UTH and admitted to NICU
iii. To compare the early infections in the newborns admitted to NICU with colonisation of the vagina and perineum in their respective mothers.

1.5 Organisation of the Dissertation

The dissertation is presented as follows:

1. Chapter One. This provides the Background of the subject of maternal bacterial colonisation of the vagina and perineum at birth and its implications and potential for newborn infection. The Statement of the Problem highlights that neonates admitted to the Neonatal Intensive Care Unit at the University teaching Hospital have the potential of being infected through labour and anecdotal evidence suggests this could be due to maternal colonisation of bacteria. The Research question, and Objectives end the Chapter 1.
2. Chapter Two is the Literature Review which summarises the relevant global, regional and the sparse local literature around the topic of maternal bacterial colonisation and the potential for newborn sepsis.
3. Chapter Three contains the Methodology. This describes the study design, the site and duration, the study population, eligibility criteria, sample size and sampling method, the data collection strategy, the variables of interest, ethical considerations and the data analysis plan and the study limitations.
4. Chapter Four includes a description of the summarised data and the accompanying tables. It includes the baseline characteristics of the study

participants and the newborns, and the laboratory results of the maternal and newborn samples tested for bacteria.

5. The Discussion which places the Results in the local, regional and international context.
6. The Conclusions based on the findings and Recommendations.

CHAPTER TWO: LITERATURE REVIEW

Most newborn deaths (98%) due to infections occurred in developing countries, mostly in Africa and Asia, while 2% occur in developed countries (WHO, 1999). Early onset infection of the newborn sets in within 24 hours of birth (WHO, 2010). Early infections of the newborns are acquired either vertically from the mothers during labour and delivery or horizontally from the hospital or community environments (Nelsons, 2013).

The incidence of newborn infections in the developed countries for instance in Australia is < 5 per 1000 live births while incidence in Africa was > 170 per 1000 live births (Thanver et al, 2009). In a global systematic review and meta–analysis Chan et al (2013i) reported that newborn babies of mothers with bacterial colonisation of the vagina and perineum had 9.4 times higher odds of laboratory-confirmed infection than newborn babies of non-colonised mothers. Their conclusion was that neonatal infections in the first week of life are associated with maternal infection and colonisation. In the United States of America (USA), clinical trials in 1970s and 1980s demonstrated that giving intrapartum intravenous ampicillin to mothers at risk was highly effective at preventing invasive Group B Streptococcal (GBS) disease in the first week of life (early-onset). In the USA, in 1996, the first national guidelines for prevention of perinatal GBS disease were developed and by the year 2002, these guidelines were revised and universal GBS screening was commenced. In the USA a multi-state population-based review of labour and delivery records in 2003-2004 found 85% of women had documented antenatal GBS screening; 98% of screened women had a colonisation result available at labour (Schraq et al, 2013). Resulting from such research findings, high intervention programs were put in place such as antenatal screening programmes which included high vaginal swabs, rectal swabs and urine cultures and the subsequent use of prophylactic intrapartum antibiotics culminating into highly reduced early neonatal infections of < 15 per 1000 births in the United States of America.

A systematic review and meta-analysis on the prevalence of early onset neonatal infection among newborns of mothers with bacterial infection or colonisation was done with a total of 122 studies meeting the inclusion criteria with only 7 studies (5.7%) from very high neonatal mortality settings. The results were as follows; the prevalence of early onset neonatal laboratory confirmed infection among newborns of mothers with

laboratory confirmed infection was 17.5% (95% Confidence Interval (CI) 6.5-27.9) with a prevalence in newborns of non-colonised mothers at 0% (95% CI 0.0-0,0). On the other hand, the prevalence of laboratory confirmed neonatal infections in newborns of mothers with risk factors of term Pre-labour Rupture of Membranes (PROM), Preterm Pre-labour Rupture of Membranes (PPROM) and Prolonged Rupture of Membranes (PRM) was 2.9-19.2%, and from surface colonisation among newborns of colonised mothers was 30.9-45% depending on the organisms (Chan et al, 2015).The conclusion from this meta-analysis was that the prevalence of early neonatal infections is high among newborns of mothers with infection or risk factors for infection and also that more high quality studies are needed particularly in high neonatal mortality settings to accurately estimate the prevalence of early onset infections in newborns.

In a systematic review and meta-analysis (Chan et al, 2013i, ii), newborns of mothers with laboratory confirmed infection had odds ratio 6.6 (95% CI 3.9-11.2) for laboratory confirmed infections themselves compared with newborns of mothers without laboratory confirmed infection while newborns of mothers with colonisation had odds ratio of 9.4 (95% CI 3.1-28.5) of laboratory confirmed infection compared with newborns of non-colonised mothers. Newborns of mothers with risk factors for infection had an odds ratio of infection of 2.3 (95% CI 1.0-5.4) compared with newborns of mothers without risk factors. A research done in Coastal Kenya looked at maternal colonisation with Streptococcal agalactiae, and associated stillbirth and neonatal disease. Maternal recto-vaginal GBS colonisation (7967 women), stillbirth and neonatal disease were assessed with results revealing low maternal GBS colonisation prevalence of (934/7967, 12%), but comparatively high incidence of GBS-associated stillbirth and early onset neonatal disease in the hospital 0.91(0.25-2.3)/1000 birth; 0.76(0.25-1.77)/1000 live births respectively (Seale et al, 2016).

The anecdotal prevalence of suspected infection of the newborns admitted to NICU from UTH labour ward stood at 62.4% (UTH NICU Reports, 2015).

Although neonatal infections cause a significant proportion of deaths in the first week of life, little is known about the burden of neonatal disease originating from maternal infection or colonisation globally.

CHAPTER THREE: RESEARCH METHODOLOGY

3.1 Study Design

This was a prospective cross-sectional study.

3.2 Study Site

Department of Obstetrics and Gynaecology at the University Teaching Hospital Labour Ward and the Neonatal Intensive Care Unit (NICU).

3.3 Target Population

All women that delivered in the labour ward at the University Teaching Hospital, Lusaka, Zambia and their newborn babies.

3.4 Study Population

Women who delivered in the labour ward at the University Teaching Hospital, Lusaka, Zambia whose newborn babies were admitted to NICU within 2 hours of vaginal delivery and who met the eligibility criterion.

3.5 Eligibility Criteria

3.5.1 Inclusion Criteria

i. Women who had spontaneous vaginal delivery at UTH labour ward
ii. Any age, parity or gestation
iii. Had a newborn admitted to NICU for any indication within two hours of birth
iv. Women who consented to participate in the study

3.5.2 Exclusion Criteria

i. Women who did not deliver at UTH and whose newborn babies were admitted to NICU.
ii. Women delivered by caesarean section
iii. Women with multiple gestation
iv. Women delivered by assisted vaginal deliveries

3.6 Sample Size

Sample size was calculated using Epi-info calculator using the prevalence formula:

$$N=\frac{Z^2 P (1-P)}{(d)^2}$$

Whereby;

N=Sample required

Z=Statistic at 95% confidence interval = 1.96

P=Expected prevalence = 6.5% (0.065) from (Chan et al, 2013, 2015).

d=Acceptable accuracy range = 0.05

The calculated sample size = 93

3.7 Sampling

Convenience sampling was used to recruit all eligible participants in the UTH labour ward.

3.8 Study Duration

Commenced July, 2017 to February, 2018

3.9 Data Collection

Key staff members in the labour ward, NICU and the laboratory, were recruited as research assistants. They were oriented and trained in the data collection tools and techniques. Mothers were provided with an information sheet (Appendix A) and informed consent was obtained (appendix B; and Appendix C for those under 18).

A structured interviewer administered questionnaire was used to collect demographic, obstetric, medical and social economical information from the participants (Appendix D). Uniformity of data collection using this tool was ensured by prior orientation training that was given to the research assistants who comprised of senior midwives working as crew leaders covering all the shifts in a twenty four hours day. The same research assistants were also oriented on how to collect and label the high vaginal and

rectal swabs from the participants using standard swabs that were provided and kept in a designated place in the labour ward. These were then placed in a designated cooler box that was clearly labelled for the research and placed at a specified area in the labour ward and sent to the UTH Microbiology Laboratory within twelve hours. It is important to note that collection of high vaginal swabs and rectal swabs was not routine practice at UTH at the time of this research and women had consented to their collection.

The collection of blood cultures from newborn babies admitted to the NICU was standard practice at UTH at the time of this research. However, an orientation of the resident doctors together with the critical care nurses in the NICU was done on how to identify eligible newborns, collect the blood cultures and label them. The recruited newborns were given matched numbers with their recruited mothers for identification and ease of tracing the matched results.

The high vaginal swabs, rectal swabs and the blood cultures all went to the microbiology laboratory for microscopy, culture and susceptibility testing. Results were entered in a book as well as in the computer and printed out accordingly. The double data entry reduced the entry errors and ensured consistent checks to be done.

3.10 Variables of interest

Table 1 below highlights the variables of interest studied and Table 2 summarises the categories.

Table 1: Variables of interest

Dependent variables; Organisms isolated in the vaginal, rectal swabs from the mothers and in the blood cultures from the newborns.
Independent variables; Participant characteristics e.g. age, gravidity, parity, gestational age, marital status, residence, HIV status, level of income Maternal conditions e.g. pre - labour premature rupture of membranes, premature rupture of membranes, prolonged rupture of membranes Newborn outcomes e.g. Apgar score, sex, birth weight

Table 2 Operational definitions of variables

Variable	Indicator	Scale of measure
Age (years)	below 19 (18 or less)	adolescent
	between 20-35	safer reproductive age
	above 35	risky reproductive age
Parity	1	primipara
	between 2-4	multipara
	5 and above	grand multipara
Gestational age (weeks)	below 37 weeks	preterm
	between 37-40	term
	above 40	post dates
HIV status	negative	protective
	Positive	risky
Education	none	uneducated
	Primary/secondary/tertiary	educated
Birth weight (kg)	above 2.5	normal
	below 2.5	low birth weight
	below 1.5	very low birth weight
	below 1.0	extremely low birth weight
Apgar score	above 8/10	normal
	between 5-6/10	moderate asphyxia
	below 4/10	severe asphyxia

3.11 Ethical Considerations

After approval at the Graduate Proposal Presentation Forum (GPPF) (Appendix E), Ethical approval was obtained from UNZABREC, Ref. NO. 013–10 -16 (Appendix F). Permission to collect data from the patients admitted in the institution was obtained from the UTH. It was made clear to the participants that their participation in the study was completely voluntary and that they were free to withdraw from the study at any point without any prejudice on their continued medical care. Participants found with infection were to be treated in accordance with the standard available treatment guidelines. Confidentiality of the participants was maintained throughout the study by keeping the consent forms separately from the data collection tools. The risk to participants in this study was less than minimal because the procedures conducted were not invasive and aseptic techniques were strictly followed during sample collection

with all procedures conducted by professional health care workers who were given prior orientation training and/or as part of standard care practiced at the UTH.

Information was given and explained in the language that the patient could understand using the information sheet (see appendix). Questions and concerns of the participants were answered and clarified using my contact details which were given. Consent form (see appendix) was administered to participants who were 18 years or older. For participants younger than 18 years, assent was collected from the participant and surrogate consent obtained from the parents or guardians.

3.12 Data Analysis

Data collected was analysed using the Statistical Package for Social Sciences (SPSS Version 22). The descriptive data of the maternal and newborn characteristics were presented in summary form. All variables were categorised appropriately (as shown in Table 2). Bivariate analysis was to be done to reflect the association of factors from mothers (e.g. parity, gestation, type of pregnancy complication, if any) that had colonisation, compared to those that did not. Subsequent Multiple Logistic Regression would have been done to show which maternal factors were independently associated with maternal colonisation. Similar analysis was to be done for the newborn infection.

However, due to the results which showed predominantly normal flora in maternal samples and negative blood culture results in the newborns, there were no comparable data sets and consequently no inferential statistics were done, hence only descriptive data analysis was done. Results were presented in form of frequency tables.

3.13 Study Limitations

1. The study did not collect vaginal and rectal swab specimens from mothers whose babies were not admitted to NICU. This would have been a comparison to those whose babies were admitted to NICU.
2. Serial blood collections were not obtained from neonates, particularly as their stay in NICU extended. Any subsequent culture could have been compared with maternal colonisation, if any.
3. A larger number of women studied may have shown a more diverse bacterial colonisation.
4. The results can not be generalised to the whole country because it was only conducted for deliveries occurring at the UTH and newborns in the UTH NICU.

CHAPTER FOUR: RESULTS

4.1 Overall baseline characteristics of the women in the study

A total of 94 mothers together with their newborns were recruited in the study after all mothers gave written consent. All their socio-demographic and pregnancy characteristics are as summarised in Table 3. The majority of the mothers 77 (81.9%) were between the ages of 18 and 35, with 14 (14.9%) above 35 years and only 3 (3.2%) below the age of 18 years. There were 82 (87.2%) married women with the rest (n=12, 12.8%) being single. The majority of the women (n=55, 58.5%) had reached secondary level of education, with 15 (16 %) attaining tertiary education, 18 (19.1%) had reached primary education whilst 6 (6.4%) had not been to school. A total of 46 (48.9%) of the participating women came from high-density areas with an equal distribution of those that came from medium and low-density areas at 20 (21.3%) respectively, while only 8 (8.5%) came from rural areas.

There were 35 (37.2%) primigravidas, 43 (45.7%) multipara and 16 (17.0%) grand multipara. Among the participating women, 74 (78.7%) were HIV negative, 10 (10.6%) were HIV positive and on treatment, 6 (6.4%) were positive and not on treatment while 4 (4.3%) did not know their HIV status.

The mothers were admitted to UTH for different reasons which included; high risk for infections (PPROM, PROM, prolonged rupture of membranes, prematurity chorioamnionitis, prolonged second stage of labour) at 35 (37.2%); anticipated difficult delivery (cephalopelvic disproportion, grand multiparity and multiple pregnancy) at 13 (13.8%); hypertensive disorders (pregnancy induced hypertension, pre-eclampsia and eclampsia) were at 15 (16%); previous caesarean section operations at 6 (6.4%); antepartum haemorrhage at 2 (2.1%); malpresentation (breech, transverse, oblique) at 3 (3.2%) and the others at 8 (8.5%).

Table 3: Baseline characteristics of the women in the study

Variable	n (N=94)	Percent
Age (years)		
Less than 18	3	3.2
18 – 35	77	81.9
Greater than 35	14	14.9
Marital Status		
Married	82	87.2
Single	12	12.8
Education		
None	6	6.4
Primary	18	19.1
Secondary	55	58.5
Tertiary	15	16.0
Residence		
High density	46	48.9
Medium density	20	21.3
Low density	20	21.3
Rural	8	8.5
Parity		
Primigravida	35	37.2
Multipara	43	45.7
Grand multipara	16	17.0
Mother HIV Status		
Negative	74	78.7
Positive on cART	10	10.6
Positive not on cART	6	6.4
Unknown	4	4.3
Gestation age (weeks)		
<28	8	8.5
29-31	17	18.1
32-36	16	17.0
37-40	38	40.4
>40	13	13.8
unknown	2	2.1
Reason for maternal admission to UTH labour ward		
Previous C/S	6	6.4
APH	2	2.1
Malpresentation	3	3.2
No complications	12	12.8
Anticipated Difficult Delivery	13	13.8
High Risk for Infection, (PPROM, PROM, prolonged rupture of membranes, prematurity chorioamnionitis, prolonged second stage of labour)	35	37.2
Hypertensive disorders	15	16.0
Others	8	8.5

4.3 Characteristics of the newborns in the study

The characteristics of the 94 newborn babies admitted to NICU is summarised in Table 4. The majority of newborns, 48 (51.1%), admitted to NICU had birth weights greater than 2.5 kg, 24 (25.5%) were between 1.6 – 2.5 kg, 18 (19.1%) weighed between 1 – 1.5kg whilst 4 (4.3%) weighed below 1kg.

The number of babies who had no Apgar score >8/10 at 1 minute were 44 (46.8%), against 21 (22.3%) with Apgar score 5-6/10 and 25 (26.6%) with Apgar score <4/10 at 1 minute respectively.

At 5 minutes, 64 (68.1%) had Apgar score >8/10 while 14 (14.9%) had Apgar score 5-6/10 and 11 (11.7%) with Apgar score <4/10. On the questionnaires, 4 (4.3%) and 5 (5.3%) of the newborns did not have their Apgar scores recorded at 1 and 5 minutes respectively.

Among the 94 newborn, 48 (51.1%) were females while 46 (48.9%) were males.

The newborns were admitted to NICU mostly for birth asphyxia 37(39.4%), prematurity 29 (30.9%), macrosomia 15 (16%) and meconium aspiration 8 (8.5%). The other reasons for admissions to NICU included high temperature, facial bruises and others

Table 4: Characteristics of the newborn babies in the study

Variable	n (N=94)	Percent
Birth weight		
Less than 1kg	4	4.3
1 - 1.5 kg	18	19.1
1.6 - 2.5 kg	24	25.5
Greater than 2.5 kg	48	51.1
Sex of newborn		
Female	48	51.1
Male	46	48.9
Apgar score at 1 minute		
Normal (>8/10)	44	46.8
Moderate Asphyxia (5-6/10)	21	22.3
Severe Asphyxia (<4/10)	25	26.6
Not known	4	4.3
Apgar score at 5 minutes		
Normal (>8/10)	64	68.1
Moderate Asphyxia (5-6/10)	14	14.9
Severe Asphyxia (<4/10)	11	11.7
Not known	5	5.3
Apgar score at 10 minutes		
Normal (>8/10)	69	73.4
Moderate Asphyxia (5-6/10)	14	14.9
Severe Asphyxia (<4/10)	3	3.2
Not known	8	8.5
Reason for newborn admission to NICU		
Poor Apgar Score/clinical asphyxia	37	39.4
Prematurity	29	30.9
Macrosomia	15	16.0
Meconium Aspiration	8	8.5
High Temperature	2	2.1
Facial Bruises	1	1.1
Others	2	2.1

4.5 Laboratory results for maternal vaginal and rectal swabs and newborn blood cultures

Of the maternal high vaginal swabs, 87 (92.6%) of the isolated organisms were normal flora whereas the remaining 7 (7.4%) consisted of 2 (2.1%)Staphylococcus epidermidis (skin normal flora), 2 (2.1%) Staphylococcus species, 2 (2.1%) Morganella morganii and 1 (1.1%) Escherichia coli. In the maternal rectal swabs, 92 (97.9%) of the isolates were normal flora whilst the 2 (2.1%) were Salmonella species, all as indicated in Table 5.

There were no organisms isolated in 93 (98.9%) of the blood cultures from the newborns apart from one (1.1%) sample where there was skin normal flora (Staphylococcus epidermidis) isolated was attributed to contamination.

Table 5: Laboratory results for maternal vaginal and rectal swabs and newborn blood cultures

Laboratory test	n (N=94)	percent
Mothers		
Vaginal Swabs		
Normal Flora	87	92.6
Staphylococcus species	2	2.1
Staphylococcus epidermidis	2	2.1
Escherichia coli	1	
		1.1
Morganella morganii	2	2.1
Mothers		
Rectal Swabs		
Normal Flora		97.9
Salmonella species		2.1
Newborns		
Blood Cultures		
No growth	93	98.9
Growth	1	1.1

4.6 Susceptibility laboratory results for the isolated organisms

The Escherichia coli and Salmonella that were isolated from the maternal high vaginal and rectal swabs demonstrated resistance to some commonly used antibiotics such as ampicillin, ceftriaxone, cefuroxime, cotrimoxazole and penicillin. The E.coli even demonstrated resistance to imipenem. However, both the E.coli and the Salmonella were susceptible to chloramphenicol. The results are as shown in Table 6.

Table 6: Susceptibility laboratory results for the isolated organisms

Isolated Organisms	Susceptibility	Resistance
▪ Salmonella species ▪ Escherichia coli	• Chloramphenicol	• Ampicillin • Ceftriaxone • Cefuroxime • Cotrimoxazole • Penicillin
▪ Escherichia coli	• Chloramphenicol	• Imipenem

CHAPTER FIVE: DISCUSSION

The key findings were that most of the isolated organisms colonising the vagina and rectum of the mothers that had just delivered a newborn that was admitted to NICU were normal flora. The susceptibility results for the few other isolated organisms revealed an increased resistance pattern to some of the commonly used antibiotics at UTH. However, there were negative findings in the blood culture results from the newborn babies admitted to the NICU. The detailed discussion of the results is given below under the different subsections.

5.1 Laboratory results

The vaginal swab results of 87 (92.6%) isolation of normal flora in the study could mean that the women in labour could not be the likely source of the high levels of infections in the newborns as previously suspected. The study found that 7 (7.4%) of the vaginal swabs had Escherichia coli, Morganella morganii, Staphylococcus species and Staphylococcus epidermidis isolated. The Staphylococcus epidermidis (normal flora for the skin) isolated was likely from the contamination from the surrounding skin. The absence of highly infectious organisms such as beta haemolytic Streptococcus and Klebsiella in the vaginal swabs confirmed that the group of women in labour were not colonised by such organisms.

The study found that 92 (97.9%) of the rectal swabs had normal flora isolations with the 2 (2.1%) with Salmonella species isolated. The absence of Klebsiella and beta haemolytic Streptococcus in the rectal swabs also was an indicator that the women in labour were not colonised by such organisms. On the overall, the negative results in the blood culture from the newborns were consequential to the non-colonisation of the mothers' vaginas and rectums by infectious microorganisms. These findings were comparable with the results in a systematic review and meta-analysis that showed a prevalence of early onset neonatal laboratory confirmed infections in newborns of non-colonised mothers at 0% (95% CI, 0.0-0.0) (Chan et al, 2013i).

The susceptibility results on the isolated organisms showed that there was resistance to some of the commonest used antibiotics at the UTH. Of note was the resistance of the Escherichia coli in the vaginal swab and the Salmonella in the rectal swabs to ceftriaxone, penicillin, cotrimoxazole and ampicillin. The E.coli isolated revealed about

50% resistance to imipenem. This result raised questions on possible evolvement of multiple drug resistant bacteria resulting from possible irrational use of antibiotics not backed by evidence. The E. coli and Salmonella were susceptible to chloramphenicol and showed a mixed susceptibility pattern to gentamycin and ciprofloxacin ranging from intermediate to resistant. This may pose future limitations on the options of antibiotics that will be available to treat these microorganisms. Jiminez et al (2012) showed that S aureus colonization (including MRSA) was extremely common (17% at enrolment between 34-37 weeks) in their cohort of 471 maternal and neonatal dyad. They reported that maternal staphylococcal colonization at enrollment increased the odds of infant staphylococcal colonization at birth, though very few developed staphylococcal disease.

The collection of blood cultures just at admission to NICU could have been too early before infection could set in and this could have contributed to the negative results. However, the negative blood culture results in the newborns reaffirmed that there was no vertical transmission of infections. The skin normal flora isolated in the 1 (1.1%) of the blood culture could be explained in terms of probable contamination at the point of sample collection. This finding, gave a good indicator of good standards of infection prevention being practiced in the NICU at the UTH in Lusaka. The negative blood culture results in babies born from the 35 (37.2%) women who had conditions of high risk for infections could have been attributed to the intrapartum antibiotics that were administered to these women as part of the standard of care in the labour ward at the UTH. This finding was unlike the findings in a meta-analysis which revealed that newborns of mothers with risk factors for infection had odds ratio of infection of 2.3 (95% CI, 0-5.4) compared with newborns of mothers without risk factors (Chan et al, 2013i). This study did not involve follow up serial blood cultures in the newborns, hence was not able to help in finding out the point at which the newborns become infected. This study did not focus on establishing the prevalence of neonatal infections in the NICU at the UTH. However, the negative blood culture results could be an important incidental finding that could be used to raise questions on the high prevalence of 62.4% of presumed sepsis from anecdotal data (UTH, NICU perinatal reports, 2015). This is in comparison to the 12% prevalence of laboratory confirmed neonatal infections in a study done in coastal Kenya (Seal et al, 2016).

The study did not isolate similar organisms colonising the maternal vaginas and rectums and in the blood cultures of the newborns admitted to the NICU. Therefore, with negative blood culture results, the study did not proceed to the use of polymerase chain reaction on the isolated organisms from the maternal vaginal and rectal swabs.

CHAPTER 6: CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

Maternal colonisation of the vagina and rectum in the population studied showed no Group B streptococcus but a predominance of normal flora.

There were no isolations in the blood cultures taken at admission from the newborns in NICU and hence it was not possible to link maternal colonisation with early newborn infections of babies admitted to NICU at the University Teaching Hospital, Lusaka, Zambia.

6.2 Recommendations

1. A larger number of women need to be studied to show a more diverse bacterial colonisation.
2. Such larger studies should also include surface swabs from the newborn.
3. Each maternity and neonatal unit to institute surveillance systems to identify maternal vaginal and perineal bacterial colonisation and links to early neonatal sepsis.
4. Antibiotic regimens in the NICU at the UTH should be constantly reviewed in line with available culture results.
5. Continued surveillance and infection prevention measure are recommended.

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APPENDICES

Appendix A: Participant Information Sheet

Title: Correlation of early infections in newborns admitted to the Neonatal Intensive Care Unit (NICU) and with those in their mothers at the University Teaching Hospital (UTH), Lusaka, Zambia.

Introduction

My name is **Dr. Whyson T. Munga,** a postgraduate student at the University of Zambia, School of Medicine. As part of the requirement for the award of, Master Degree in Medicine, Obstetrics and Gynaecology, I am hereby conducting a research on the above subject at UTH, Departments of Obstetrics and Gynaecology and Paediatrics and Child Health. I am kindly inviting you to take part in this study. You are being asked to take part in this study because your newborn baby has been admitted to Neonatal Intensive Care Unit.

Purpose

It has been noted that many newborn babies that get admitted to the Neonatal Intensive Care Unit at UTH die mostly due to infections whose source is not yet known. It is with this view that at the end of this study, I would like to find out, the link between the infections noted in the newborns in NICU and those in their mothers at UTH. The information collected will help in coming up with methods of improving hygienic standards of preventing infections during deliveries or specific treatment of mothers during delivery so as to reduce or prevent infections in the newborn babies. This study will serve as a basis for future research in maternal infections during labour and delivery.

Explanation of the procedure

You have been invited to this study because we want to know the association between the infections in newborns admitted to NICU and in their mothers during delivery. If you agree to take part in this study, you will be asked some questions to help us know you better. Your vagina and rectum will be swabbed to enable us find out what organisms are found there. Take note that swabbing for specimen purposes is not routine procedure when women come in labour.

Blood will be collected from your newborn when admitted to NICU (done routinely on every admitted newborn) to find out what organisms are found there. The specimen collected from you and your newborn admitted to NICU will be sent to the laboratory within UTH where tests will be conducted to look for the presence of microorganisms using microscopes. If disease causing organisms will be found in these specimens, they will be exposed to different medicines so as to find out which medicine can be used to treat the infection caused by the identified organisms. If infection will be found in the specimen collected from you and your newborn, specific treatment will be given to both of you following the standard treatment guidelines available for such infections. The organisms found in you and in your newborn will be compared to find out if they are the same. I wish to state that there is nothing new that will be administered to you. Your labour will be managed according to the standard of care at this hospital. Your participation is voluntary and you are free to withdraw from this study at any time and you will still receive the standard medical care.

Benefits

The benefit to the participants in this study is that if they will be found with infection, treatment will be given to them following the available treatment guidelines for such infection. However, there is no monetary or any direct benefit/incentives to the participant by virtue of participating in this study because your labour and delivery will be managed as per hospital standard here at UTH.

Risks

The risk to participants in this study is less than minimal, because apart from swabbing your vagina and rectum, nothing new will be administered to you.

Confidentiality

The information collected will be kept confidential. The samples collected, the research findings will not bear your names such that no one will know about you.

Consent

If you agree to take part, please sign the consent form which will allow us to enrol you in this study. If you have any questions or clarifications to make, please contact the addresses below;

Dr. Whyson T. Munga,
University Teaching Hospital
Department of Obstetrics and Gynaecology
Private Bag RW 1X
Lusaka
Phone **+260 979 511 645**
Email Address: **whysonmunga@yahoo.co.uk**

OR

The Chairperson,
The University of Zambia Biomedical Research Ethics Committee (UNZABREC)
School of Medicine,
Ridgeway Campus – Basic Sciences Building First floor
Nationalist Road,
P.O. Box 50110,
Lusaka.
Telephone: +260 – 1 – 256 067, E – mail: unzarec@unza.zm

Appendix B: Participant Consent Form

Title: Correlation of early infections in newborns admitted to the Neonatal Intensive Care Unit (NICU) and with those in their mothers at the University Teaching Hospital (UTH), Lusaka, Zambia.

I have read and I clearly understand all that is involved in this study. I therefore, voluntarily agree to participate in this research.

---	---	---
Name of participant	Signature/Thumb	Date
---	---	---
Name of witness	Signature/Thumb	Date
---	---	---
Name of researcher	Signature/Thumb	Date

NB: Consent forms to be kept separate from data collection tools so as to ensure maintenance of confidentiality.

Appendix C: Assent Form for Participants below 18 Years Old

Title: Correlation of early infections in newborns admitted to the Neonatal Intensive Care Unit (NICU) and with those in their mothers at the University Teaching Hospital (UTH), Lusaka, Zambia.

I have read and I clearly understand all that is involved in this study. I (Name) ---------- (Relationship with the participant) ---------- therefore, on behalf of my relative ---------- do voluntarily agree that she can participate in this research.

----------	----------	----------
Name of Proxy	Signature/Thumb of the Proxy	Date
---------- -	----------	----------
Name of witness	Signature/Thumb	Date
----------	----------	----------
Name of researcher	Signature/Thumb	Date

NB: Assent forms to be kept separate from data collection tools so as to ensure maintenance of confidentiality.

Appendix D: Study Questionnaire

Title: Correlation of early infections in newborns admitted to the Neonatal Intensive Care Unit (NICU) and with those in their mothers at the University Teaching Hospital (UTH), Lusaka, Zambia.

File #:_____ Name _____ Age _____

Marital Status _____ Religion_____ Para_____

Gestational Age at delivery_____

Reason for referral to UTH_____

Birth Weight of the baby_____

Phone number #:_____

1. What is the level of your education?

0. None ( )

1. Primary ( )

2. Secondary ( )

3. Tertiary ( )

2. Are you employed?

0. Not employed ( )

1. Informal ( )

2. Formal ( )

3. Residence (write name of place of stay) _____

0. High density ( )

1. Medium density ( )

2. Low density ( )

3. Rural ( )

4. What is your net monthly income in Zambian Kwacha?

0. 0 - 1,000 ( )

1. 1, 00 - 2,000 ( )

2. 2,001 - 4,500 ( )

3. > 4,500 ( )

5. What is your HIV status?

0. Unknown ( )

1. Negative ( )

2. Positive not on cART ( )

3. Positive on cART ( )

6. What is the foetal outcome?

Apgar Score At 1min____ 5min ____ 10 min____

Birth weight _____

Sex of the New-born

Female ( )

Male ( )

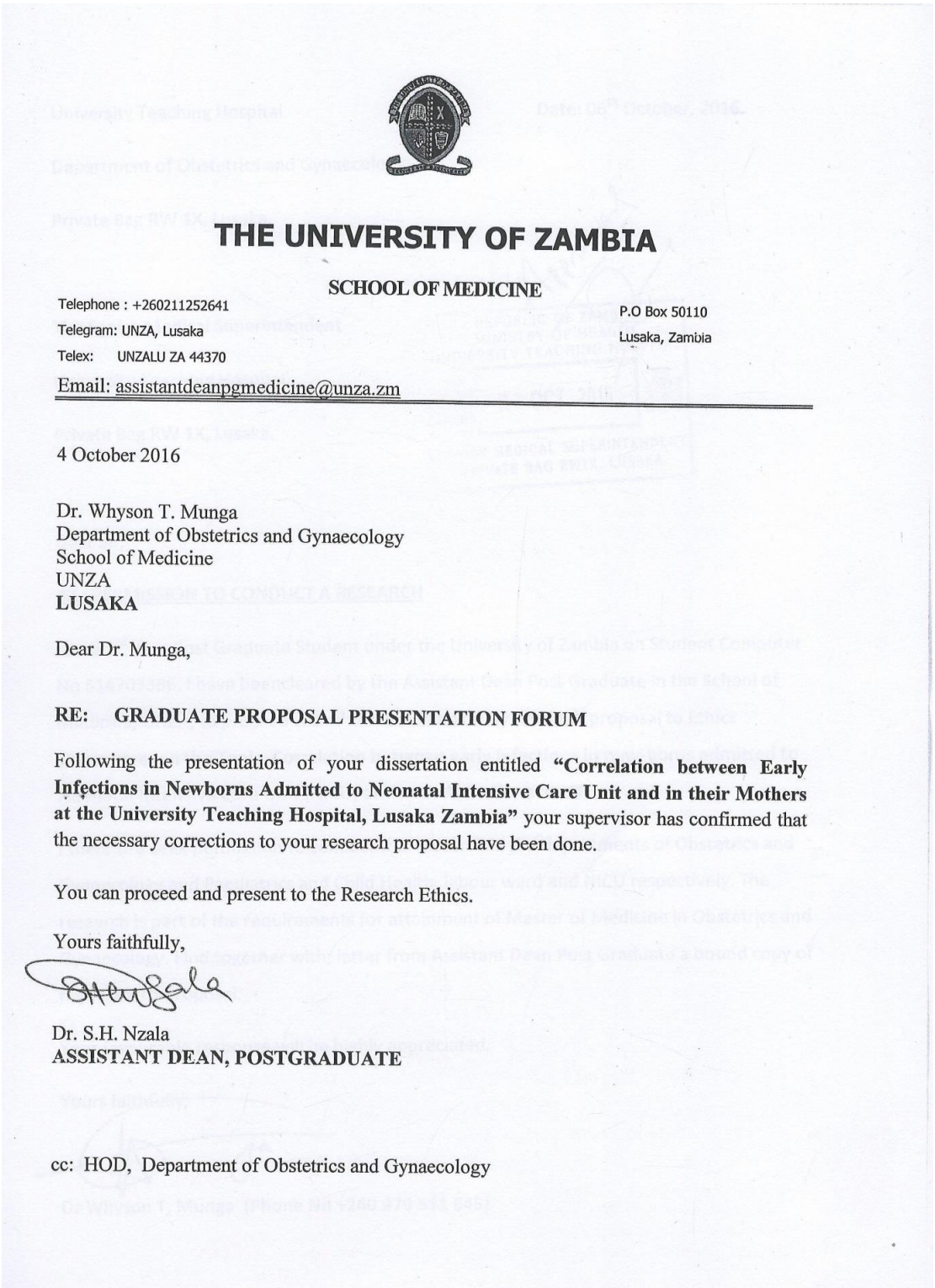
7. Reason for admission to NICU?

_____

_____

Please tick or write the information in the appropriate space.

Appendix E Approval letter from GPPF



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4 October 2016

Dr. Whyson T. Munga
Department of Obstetrics and Gynaecology
School of Medicine
UNZA
LUSAKA

Dear Dr. Munga,

RE: GRADUATE PROPOSAL PRESENTATION FORUM

Following the presentation of your dissertation entitled **"Correlation between Early Infections in Newborns Admitted to Neonatal Intensive Care Unit and in their Mothers at the University Teaching Hospital, Lusaka Zambia"** your supervisor has confirmed that the necessary corrections to your research proposal have been done.

You can proceed and present to the Research Ethics.

Yours faithfully,

Dr. S.H. Nzala
ASSISTANT DEAN, POSTGRADUATE

cc: HOD, Department of Obstetrics and Gynaecology

Appendix F: Approval letters from Ethics Committee

THE UNIVERSITY OF ZAMBIA

BIOMEDICAL RESEARCH ETHICS COMMITTEE

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Ridgeway Campus
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Lusaka, Zambia

Assurance No. FWA00000338
IRB00001131 of IORG0000774

15th December, 2016.

Our Ref: 013-10-16.

Dr. Whyson Munga,
University Teaching Hospital,
Department of Obstetrics and Gynaecology,
P/Bag RW 1X,
Lusaka.

Dear Dr. Munga,

RE: RESUBMITTED RESEARCH PROPOSAL: **"CORRELATION BETWEEN EARLY INFECTIONS IN NEWBORNS ADMITTED TO NEONATAL INTENSIVE CARE UNIT AND IN THEIR MOTHERS AT THE UNIVERSITY TEACHING HOSPITAL, LUSAKA, ZAMBIA." (REF. NO. 013-10-16)**

The above-mentioned research proposal was presented to the Biomedical Research Ethics Committee on 12th December, 2016. The proposal is approved.

CONDITIONS:

- This approval is based strictly on your submitted proposal. Should there be need for you to modify or change the study design or methodology, you will need to seek clearance from the Research Ethics Committee.
- If you have need for further clarification please consult this office. Please note that it is mandatory that you submit a detailed progress report of your study to this Committee every six months and a final copy of your report at the end of the study.
- Any serious adverse events must be reported at once to this Committee.
- Please note that when your approval expires you may need to request for renewal. The request should be accompanied by a Progress Report (Progress Report Forms can be obtained from the Secretariat).
- **Ensure that a final copy of the results is submitted to this Committee.**

Yours sincerely,

Dr. S.H Nzala
VICE-CHAIRPERSON

Date of approval: 15th December, 2016. **Date of expiry**: 14th December, 2017.