

JNMC WOMEN'S AND CHILDREN'S HEALTH RESEARCH UNIT

KLE Academy of Higher Education and Research's J. N. Medical College, Belagavi

In **1999**, an academic collaboration was established between JNMC and University of Illinois at Chicago, USA with the objective of strengthening Medical Education as well as to develop research capacity and clinical care services in Maternal and Child Health.

The National Institute of Child Health and Human Development of the National Institutes of Health, USA for the first time ever formed a **Global Network for Women's and Children's Health Research** in the year **2001** to implement community based research studies to improve maternal, neonatal, infant and early childhood health and accelerate the achievement of Millennium Development Goals 4 and 5 (of reducing maternal and newborn mortality) in low and middle income countries across Asia, Africa and Latin America. The initiative was generously supported by the Bill & Melinda Gates Foundation. In response to this initiative, JNMC, in collaboration with UIC, submitted a research proposal for funding and was selected as one of the original ten sites in the network from India, Pakistan, Tibet, Zambia, Democratic Republic of Congo, Argentina, Uruguay, Brazil, and Guatemala for the initial five years of funding. **JNMC is the only private institution to receive this research grant.** Realizing the Global Network mandate, JNMC established a Women's and Children's Health Research Unit in 2001. Building on the expanded research capacity emanating from Global Network participation, JNMC has forged collaborations with nine Universities of the USA and two from Canada as well as other international not-for-profit organizations. This has enabled the creation of an international multi-disciplinary research team of clinicians, scientists, public health experts, and information technology specialists supporting the development of research protocols, the results of which have global impact on the health of women and children. Based on its commendable performance during the first cycle, the 'Research Unit' gained recognition as one of the six among the ten sites to be re-funded for a third cycle of five years until 2018 and this has been further continued in the fourth cycle of funding until 2023.

The establishment of '**Women's and Children's Health Research Unit**' at JNMC has been supplemented by essentials like the setting up of five regional data centres throughout the district, training of dedicated research faculty and the strengthening of Institutional Review Board mechanisms in order to accomplish research capacity building and infrastructure development. The research unit has developed a Study Management System, comprising electronic data entry and management, for monitoring the process evaluation. In fulfilment of its mission, the research unit has forged a strong **Public Private Partnerships** with the Belagavi District Health Administration for implementing community based interventions and presently serves a population of over **670,000** residing in **231** villages spread over eight talukas of Belagavi district. This population is served by **32** Primary Health Centers and the health workers have been trained for ethical conduct of research and data collection. This community based research network offers an ideal platform for testing evidence based intervention for impacting health outcomes of this under-served population.

Over the past eighteen years, JNMC's multi-disciplinary research team has conducted a number of community based research projects with support from World Health Organization, Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Global Network for Women's and Children's Health Research, other NIH agencies, Bill & Melinda Gates Foundation, American Academy of Pediatrics, Gynuity Health Projects, Thrasher Research Fund, Department of

Biotechnology Govt. of India and the UK Medical Research Council. The results of these insightful research studies have had a profound impact at national and international levels in shaping public health policies.

Research Priorities

- **Surveillance System** – Maternal Newborn Health Registry (MNHR)
- **Maternal Health** – Postpartum Hemorrhage (PPH), Hypertensive Disorders of Pregnancy (HDP), Maternal Nutrition, Maternal Sepsis
- **Newborn Health** – Birth Asphyxia, Preterm Birth, Infant Neurodevelopment, Newborn Sepsis
- **Health System Strengthening** – Emergency Obstetric and Neonatal Care (EMONC)

Maternal Newborn Health Registry

The '**Maternal Newborn Health Registry (MNHR)**' an essential component of the Global Network, is a prospective, population-based observational study to quantify trends in pregnancy outcomes, including stillbirths and neonatal and maternal mortality rates, in geographically defined low-resource areas. It has operated since 2008, enrolling all pregnant women residing in defined study clusters and tracking birth outcomes through 6 weeks post-delivery. As a part of registry, annual household survey is undertaken and all the eligible couples and Likely-to-Conceive women enlisted at every village level. They are being tracked by Accredited Social Health Activist (ASHA) and Registry Administrators (RAs) every month for early identification of the pregnancy and subsequent enrolment. This unique systematic tracking has been the baseline for many research protocols targeted to test the interventions for reducing maternal and newborn morbidity and mortality. The network's registry has the data of nearly 6,80,000 maternal and neonatal outcomes and Belagavi site has contributed more than 25% of the data with 1,72,000 outcomes as on October, 2019.

Research Studies Related to Maternal Health

JNMC Women's and Children's Health Research Unit has conducted many trials related to the maternal health in the areas of Postpartum Haemorrhage, Hypertensive Disorders of Pregnancy, Maternal Nutrition and Maternal Sepsis.

Postpartum Haemorrhage

The first research project launched by the research unit was the community-based first ever placebo controlled, "Randomized controlled Trial of Oral Misoprostol for prevention of Postpartum Haemorrhage in women delivering at homes or sub-centres of four Primary Health Centre Areas of Belagavi District". **Misoprostol** is now endorsed by the Government of India for community level prevention of postpartum bleeding. The Belagavi site was the first GN site to initiate and complete data collection for the primary trial from September 2002 to December 2005. The primary publication arising from this trial was published in the October 7, 2006 issue of 'The Lancet'. This study provided the critical evidence for the inclusion of Misoprostol on the World Health Organization's List of Essential Medicines for prevention of postpartum haemorrhage and stronger advocacy of Misoprostol for PPH prevention by the United Nation's Commission on Life-saving commodities for maternal

health. It also prompted expansion of the registration and use of Misoprostol for prevention of postpartum bleeding, by the Ministries of Health of 26 countries.

The skill of birth attendants in conducting delivery and management of the immediate postpartum period is a critical factor in determining the extent of blood loss after childbirth. Following the successful implementation of the Misoprostol trial, JNMC was identified by **World Health Organization** and the **Ministry of Health, Govt. of India** as nodal centre to develop modules for training Medical Officers and Auxiliary Nurse Midwives as well as the faculty of medical colleges in Karnataka in **“Skilled Birth Attendance”**. The trained faculty in turn has trained the Medical Officers working at 24 x 7 Primary Health Centers within their district. JNMC was entrusted with the responsibility of training Medical Officers of Belagavi District. The project was completed in December 2007.

In a project implemented during May 2003-April 2004, the ‘Research Unit’ developed a unique under-buttock blood collection drape with a calibrated receptacle for measuring postpartum blood loss for the Misoprostol trial. The BRASSS-V drape being more accurate than visual estimation of blood loss has particular utility for prompt detection of PPH and aids reduction of maternal morbidity and mortality in low resource settings. The drape, acknowledged by the international research community as a valid tool for measurement of postpartum blood loss, has been used in over 20 countries for measuring blood loss in over 200,000 women.

JNMC Research Unit conducted a subsequent Misoprostol trial **“Two community strategies comparing use of Misoprostol for early treatment/secondary prevention to primary prevention for postpartum haemorrhage: a randomized cluster non-inferiority study in Bijapur district, Karnataka, India”** in collaboration with Gynuity Health Projects, New York, USA, University of Illinois at Chicago, and University of California at San Francisco with funding from Bill & Melinda Gates Foundation, USA during January 2011 to August 2013. BLDE Deemed University's Sri B. M. Patil Medical College, Bijapur, India was the implementing partner for the study.

Active Management of the Third Stage of Labour (AMTSL) reduces the occurrence of severe postpartum haemorrhage by approximately 60-70%. Controlled cord traction is one of those components of AMTSL which if implemented efficiently through proper training would have major implications for effective management of the third stage of labour at peripheral levels of health care. The World Health Organization took the initiative to address this important public health issue through the **“Active Management of the Third Stage of Labour without Controlled Cord Traction: A Randomized Non-Inferiority Controlled Trial”**. This hospital-based, multi-centre, individually randomized controlled trial, recruited 25,000 women delivering vaginally in health facilities in eight countries - Argentina, Egypt, India (JNMC), Kenya, Philippines, South Africa, Thailand and Uganda. Of these, the India site at J N Medical College, Belagavi enrolled 3,000 women at the affiliated KLES Dr Prabhakar Kore Hospital & Medical Research Center and the Primary Health Centers – Kinaye and Handiganur. The findings of this trial suggested that the control cord traction could be safely omitted from the bundle of AMTSL.

Pursuing the quest for an “ideal uterotonic” in the prevention of PPH, one that matches the efficacy of Oxytocin but that is not heat labile, a **CHAMPION Trial** sponsored by the Department of Reproductive Health & Research, World Health Organization, Geneva, in partnership with Merck for Mothers was conducted between 2014 to 2017. The clinical trial **“A phase III, randomized, double-**

blind, active, controlled, multinational, multi-center, non-inferiority trial using carbetocin room temperature stable (RTS) for the prevention of postpartum haemorrhage during the third stage of labour in women delivering vaginally” was designed to evaluate a new, proprietary heat stable formulation of Carbetocin. The Belagavi Research Unit and researchers from a total of twelve countries recruited nearly 30,000 subjects for a randomized trial conducted independently by WHO as part of its maternal and perinatal health research program (HRP) for the prevention and treatment of leading causes of maternal mortality. Notably, Belagavi site led the trial in six centers spread across different regions of India and contributed nearly a quarter of the total sample size to the trial. This landmark trial drew the attention of global community as a result of which the **British Broadcasting Corporation (BBC)** provided a platform to discuss the salient features of the trial results. The results of this trial necessitated the updating of **WHO recommendations Uterotonics for Prevention of Postpartum Haemorrhage** in December 2018.

Adherence to the recommendations and guidelines by WHO is currently limited by a number of challenges. Survey data from Kenya, Nigeria, and India show that tranexamic acid (TXA) is used late and most often for women requiring surgery for PPH. Other easy-to-implement interventions of standard PPH care, e.g., uterine massage and IV fluids, that could be critical are inconsistently used and may be considered optional by doctors and midwives. Thus with an aim to change provider behaviors so that they detect PPH early and rapidly implement all components of the bundle of care for PPH prevention viz., **Early detection, Massage of Uterus, Oxytocic drugs, Tranexamic Acid, IV fluids, Examination of Genitalia and Escalation of Care for Management of PPH (E-MOTIVE)** bundle of care. Therefore, the introduction of E-MOTIVE in LMICs is likely to necessitate co-intervention strategies to improve implementation and uptake. The behavioural and implementation sciences offer frameworks that outline the range of potential types of intervention strategies that can be used to change clinical practice behaviours and improve implementation. The primary outcome of **Understanding Effectiveness of Implementation of a PPH Initial Response Bundle** is a 25% reduction in severe PPH, laparotomy for bleeding, or mortality from bleeding, through a cluster randomized trial across 60 health facilities (276,000 women) in Kenya, Tanzania, Nigeria, South Africa, and India. In India, it will be implemented in 16 taluka hospitals of Belagavi, Bagalkote and Vijayapura Districts. This study will be conducted in collaboration with University of Birmingham, UK with funding from Bill & Melinda Gates Foundation, USA.

Hypertensive Disorders of Pregnancy

The JNMC research team in collaboration with S Nijalingappa Medical College, Bagalkote and University of British Columbia, Vancouver, Canada is engaged in implementing a series of studies at Belagavi and Bagalkote districts; collectively referred to as the **‘Community Level Interventions for Pre-Eclampsia (CLIP)’** as part of **PRE-EMPT initiative** of the Bill & Melinda Gates Foundation. CLIP Trials included a study to determine baseline rates of preeclampsia in Karnataka State, an assessment of community health worker knowledge and management of preeclampsia, and a community-based cluster randomized controlled trial (RCT) to determine if a community-based package of care for women with hypertensive disorders of pregnancy can improve maternal and neonatal outcomes. Dr Prabhakar Kore, Chancellor of KLE University and Chairman, KLE Society inaugurated the research project in Delhi on November 12, 2013. More than 100 leading public health researchers in the area of maternal health from 13 countries including the representatives of WHO, Geneva and ICMR, New Delhi attended. The CLIP definitive Trail was conducted from November 2014 to October 2016. Data

analysis was recently completed for the RCTs of all participating sites. Publications and dissemination meetings are planned to share study results.

Microlife CRADLE, a semi-automated device that was used in the CLIP Trial for detection of hypertension was tested in rural Africa and within India by the JNMC and King's College, London collaborative research team to further develop the device as an accurate and low-cost means to improve antenatal detection of pre-eclampsia as well as hypotension associated with postpartum haemorrhage and sepsis. The trial '**CRADLE 3 (Community Blood Pressure Measurement in Rural Africa and Asia: the Detection of Underlying Pre-eclampsia and Shock) Stepped-Wedge Randomised Control Trial**' in India was co-funded by the United Kingdom Medical Research Council and the Government of India, Department of Biotechnology. Notably, the India **CRADLE trial received the first ever Newton Prize for excellent research and innovation** in support of economic development and social welfare in Newton Fund partner countries. This device was one of 30 (among 500) high impact innovations to save lives Reimagining Global Health, Innovation Countdown 2030 initiative.

The CRADLE-4 Trial: Planned early delivery versus expectant management to reduce adverse pregnancy outcomes in pre-eclampsia in a low and middle-income setting has been planned to evaluate the intervention to reduce maternal mortality and morbidity based on a composite of outcomes during pregnancy and delivery, until primary hospital discharge and the impact of the intervention on short term neonatal outcomes in India (Belagavi and Bagalkote) and Zambia.

Promoting MITS activities to determine cause of death among neonates and stillbirths in tertiary care teaching hospital project will be nested in this trial. This study will utilize Minimally invasive tissue sampling (MITS), also known as minimally invasive autopsy, involves post-mortem collection of fluid and solid tissue samples using biopsy needles as an alternative to complete diagnostic autopsy which is the "gold standard" for ascertaining cause of death.

Maternal Nutrition

Nutritional deficiency poses the greatest challenge to early infant growth and development. Many strategies have been undertaken to address the widespread nutritional deficiencies of zinc and iron in older infants and toddlers. Sprinkles™ are a form of micronutrient supplement which is added to foods prepared in the home at the time of consumption; the micronutrient composition typically provides iron, zinc, and varying types and amounts of other micronutrients. To inform the choice of doses of zinc and iron in Sprinkles™ the research unit implemented a trial "**A Comparison of Two Iron Doses on Zinc Absorption from Sprinkles as Micronutrient Supplement**".

The Global Network partnership between the University of Colorado, Denver and Guatemala site developed a trial "**Women First: Pre-conception Maternal Nutrition Trial**" to assess the benefits to the offspring of ensuring optimal maternal nutrition using micro and macro nutrient supplementation prior to conception compared to initiating the same supplementation beginning at 13 weeks of pregnancy and to providing pregnant women only standard of care without nutritional intervention. A second study phase is now active and designed to assess growth and development of offspring at various age intervals up to 24 months. Four Global Network sites (Belagavi, India; Guatemala; the Democratic Republic of the Congo; and Pakistan) have participated in this study funded by the Bill & Melinda Gates Foundation. The results suggested that in resource-poor rural or semirural populations in which there is a high prevalence of stunting, fetal growth was improved with maternal nutrition

supplements commenced either before conception or late in the first trimester and provided to women irrespective of their own nutritional status.

JNMC Research Unit was involved in the conduct of study on **“Zinc and Iron bioavailability from bio-fortified pearl millet”** in collaboration with University of Colorado Health Sciences Center, USA and sponsored by International Atomic Energy Agency, Vienna. The results demonstrated that quantities of both iron and zinc absorbed when iron and zinc bio-fortified pearl millet is fed to children aged 2 years as the major staple food, is more than adequate to meet the physiological requirements for these micronutrients.

Tobacco Use among Pregnant Women

The research unit participated in a multi-site study, **“Survey of Tobacco Use among Pregnant Women”**. The overall aim of this survey was to determine the prevalence of use of tobacco products including smokeless tobacco during pregnancy as well as ascertain the knowledge and beliefs regarding the hazards of tobacco products on the mother and child. National Cancer Institute was one of the co-sponsors of this study. Although, the prevalence of tobacco smoking was very low in the study population, the use of smokeless tobacco during pregnancy and exposure to second-hand smoke in the family were significantly high. Further, awareness of the hazards of exposure to tobacco, both smoking and smokeless, on the mother and the newborn was also low, thus calling for renewed efforts to address the same. The primary publication arising from this study was selected for Faculty of 1000 Medicine for the year 2008.

Cervical Cancer Prevention

The ‘Research Unit’ has diversified its research activities and is developing capacity and infrastructure, recruitment and retention strategies for undertaking clinical research related to prevention methods for cervical cancer among HIV-infected women in Belagavi district through the **“HIV – Cervical Cancer Prevention Research Project”**. A **“Preventive Gynaecologic Oncology Unit”** that has been set up at KLES Dr Prabhakar Kore Hospital and Medical Research Center, with substantial support from the grant. This facility is equipped with a colonoscopy unit for diagnosis of cervical cancer and offers ‘Loop Electrosurgical Excision Procedure’ for women diagnosed to have pre-cancerous lesions. As a member of the consortium led by National AIDS Research Institute, Pune, this unit emerged as a nodal centre for implementing trials focused on prevention and treatment of cervical cancer.

The WHO Guidelines for screening and treatment of precancerous lesions for cervical cancer prevention recommends a screen-and-treat approach for cervical cancer prevention, with cryotherapy being the first choice of treatment for women with a positive screen. **The Performance, Safety and Efficacy of a New Cryotherapy Device for Cervical Dysplasia in Low and Middle Income Countries Study** has been initiated to determine the performance characteristics of a new cryotherapy device, **CryoPop**, compared to standard cryotherapy equipment in women with normal cervical cytology. The study will be implemented at J N Medical College, Belagavi; Karnataka Institute of Medical Sciences (KIMS), Hubli and Karnataka Cancer Therapy and Research Institute (KCTRI), Hubli with the support of Johns Hopkins University (JHPIEGO), Baltimore, USA.

Maternal and Neonatal Sepsis Prevention

Maternal and neonatal infections are among the most frequent causes of maternal and neonatal deaths. These deaths from infections are not decreasing compared with deaths from other frequent causes of mortality. The JNMC Research Unit is implementing Global Network for Women's and Children's Health Research's common Protocol "**Prevention of Maternal and Neonatal Death/Infections with a Single Oral Dose of Azithromycin in Women in Labor (in Low- and Middle-income Countries): a Randomized Controlled Trial**" aimed at addressing the frequent but neglected cause of maternal and neonatal morbidity and mortality. The trial is implemented in two General (Taluka) Hospitals viz. Bailhongal and Hukkeri, S N Medical College Shri HSK Hospital, Bagalkote and BLDEU Shri B M Patil Medical College Hospital, Vijayapura with a Grant Support from Bill & Melinda Gates Foundation. The trial also comprises of a Pilot Phase and Antimicrobial Resistance Substudy.

Research Studies Related to Newborn Health

The areas of the research related to newborn health included the most common causes of newborn morbidity and mortality viz. Birth Asphyxia, Preterm Birth and Infant Neurodevelopment, Breast feeding support.

Birth Asphyxia

In order to address the issue of birth asphyxia, one of the leading causes of early newborn mortality, the 'Global Network' between 2005 and 2008 launched a major initiative of training community - based birth attendants in Neonatal Resuscitation for reducing early neonatal mortality in developing countries. The "**First Breath: Community Based Training and Intervention in Neonatal Resuscitation**" project was implemented at seven Global Network Sites located in South Asia, Africa and Central and South America including J N Medical College, Belagavi. Nearly 90 communities, 26 of them in Belagavi District, defined as geographical medical service-based area with approximately 500 births per year, participated in the study aimed at comparing the efficacy of **Neonatal Resuscitation Program (NRP)** of the **American Academy of Paediatrics** with the **Essential Newborn Care Course** of the **World Health Organization (WHO)** in reducing early neonatal mortality. More than 65,000 births, approximately 26,000 of them in 298 villages with a population of more than 890,000 in Belagavi District, were assessed over the two and half year study period at the participating GN sites. As part of the trial, over 1,100 birth attendants including Private Practitioners, Nurses, Auxiliary Nurse Midwives and Traditional Birth Attendants were trained for newborn resuscitation on three occasions.

The encouraging results of "First Breath: community based training and intervention in neonatal resuscitation" led to the revision of the Neonatal Resuscitation Program (NRP) by the American Academy of Paediatrics (AAP) for community settings. The JNMC Research Unit was one of the five global sites selected by AAP for field testing the Helping Babies Breathe (HBB) curriculum. "**Field Implementation of Helping Babies Breathe**" project trained over 1,200 birth attendants working in 25 public sector (District Hospital, Belagavi, 7 Taluka hospitals, 2 community health centres and 15 primary health centres) and 8 private sector hospitals of Belagavi district for demonstrated resuscitation. Subsequently, HBB was incorporated into the neonatal resuscitation training curriculum of the Basic Newborn Care and Resuscitation program called "**Navajat Shishu Suraksha Karyakram**" (NSSK) of the Government of India. The Research Unit participated in the Global Network trial '**Evaluation of HELPING BABIES BREATHE in Belagavi, Kenya and Nagpur: Does implementation of HELPING BABIES BREATHE Save Lives?**' to test the effectiveness of the HBB curriculum in saving lives.

The primary publication emanating from that trial was published in BMC Pregnancy and Childbirth in August 2016. As part of the HBB trial, a mobile-based application was developed to assess if resuscitation began within the appropriate timeframe.

Preterm Birth

All research sites active in the Global Network including JNMC in 2011 implemented the ***Trial of the Use of Antenatal Corticosteroids in Developing Countries (ACT Trial)***, an 18 month cluster randomized study between October 2011 and March 2014 to assess the feasibility, effectiveness, and safety of a multifaceted intervention designed to increase the use of antenatal corticosteroids among women at risk for preterm birth at all levels of health care in low-income and middle-income countries. Although the intervention effectively increased the use of antenatal corticosteroids there was unexpected increased mortality among babies delivered at term by mothers who had received ACS suspected to be high-risk for preterm delivery. These results prompted WHO to consider the available evidence on potential benefits of ACS were largely derived from higher-level hospitals in high-resource countries and the possible harms of expanding ACS coverage in resource-limited countries to guide its 2015 recommendations on ACS. There is important uncertainty as to whether antenatal corticosteroids (ACS) are safe and/or efficacious when used in facility settings in low-resource countries. WHO is coordinating the conduct of two concurrent trials on the efficacy of antenatal corticosteroids in women at imminent risk of early and late preterm birth ‘**The WHO Antenatal Corticosteroids for Improving Outcomes in Preterm Newborns (WHO-ACTION) trials**’. This is a parallel, two-arm, double-blind, randomized, placebo-controlled trial being implemented in 5 countries, 6 sites and 26 hospitals in Bangladesh, India (JNMC Research Unit), Kenya, Nigeria and Pakistan. Trial activities will be facility-based, with community follow up of recruited women and newborns to 28 completed days.

JNMC research unit participated in “**Clindamycin to reduce preterm birth in low resource setting: A randomized placebo controlled trial**” in collaboration with Christiana Care Health Services, USA with funding from Thrasher Research Fund to assess if pregnant women in rural areas with high vaginal pH levels that were treated with Clindamycin, were less likely to deliver preterm infants than pregnant women, also having high pH levels, who received a placebo. However, the study results found that this strategy did not decrease the rate of preterm birth in a rural community-based setting in India. The study also suggested that routine screening for an abnormal vaginal microbiome and treatment with clindamycin should not be undertaken in clinical practice.

The Global Network implemented a multi-centric trial of “**Aspirin Supplementation for Pregnancy Indicated Risk Reduction in Nulliparous Women (ASPIRIN)**” to study the effects of low dose aspirin on prevention of preterm labour at the research sites of the Global Network for Women’s and Children’s Health Research. The Thomas Jefferson University-Christiana Care Health Services-J N Medical College collaborative research team is the lead investigator group that enrolled nearly 12,000 pregnancies for this placebo controlled trial. The objective of this Global Network study is to assess if low-dose aspirin administered to nulliparous, pregnant women beginning early in pregnancy can reduce preterm birth. This study has been implemented among the 16 PHC Clusters at Belagavi along with other GN Sites. Protocol Training for the ASPIRIN Trial Co-ordinators from the Global Network sites – India, Kenya, Zambia, Democratic Republic of Congo and Guatemala – was held at Belagavi during 14th to 18th November, 2016. The results of the trial are underway for publication in the Lancet.

JNMC Research unit is participating in “**Study of Cause of Death among Preterm Birth: Asia**” in collaboration with RTI International, USA and J J M Medical College Davanagere with funding from Bill & Melinda Gates Foundation, USA. The primary objective of the project is to conduct a prospective study in Asia (Karachi, Pakistan, and Belagavi, India) to determine the cause of deaths among preterm births (both live births and stillbirths). Secondary outcomes include determining the specific pathogens responsible for infection-related deaths, potential preventability of these deaths and interventions which may be effective in reducing mortality. The trial expected to complete enrolment by February 2020.

Infant Neurodevelopment

While 'First Breath' attempted reduction of early newborn mortality from birth asphyxia, it was speculated that the survivors may end up with varying degree of impaired neurological development. The burden on families and the communities assumes greater significance in view of the scarcity of supportive care available to children of rural population. The "**Brain Research to Ameliorate Impaired Neuro Development: Home-based intervention Trial (BRAIN HIT)**" addressed this concern by testing the feasibility of a home based early intervention program on babies resuscitated from birth asphyxia in improving their physical, mental and social development. The expertise developed by the home-based counsellors will be utilized for providing centre-based support to families of babies that have been successfully resuscitated. BRAIN-HIT study findings demonstrate that simple home based strategies could be effective in reducing neurodevelopment disabilities in young children from low and middle income countries.

The impact of maternal nutrition on neurodevelopment and growth of the offspring remains a potential trust area for research. ‘**Women First: Neurocognitive Development Assessment at 24 months of Age**’ study is looking at Neurodevelopment of offspring of mothers who received Nutrition Supplement during Preconception or Prenatally in Four Low Resource Settings to examine the effects of the maternal nutrition intervention in the Women First trial (WF:PMN Trial) on multiple domains of neurodevelopment in the offspring at 2 years of age. Impaired neuro-cognitive development (ND) is very common in young children in low-middle income countries (LMIC) and represents a significant loss of human potential. The extent to which improved maternal nutrition, including during preconception period and/or the prenatal period, impacts offspring is unknown and therefore limits the development of effective interventions. The trial is being implemented to address this issue.

The **Sit Down and Play (SDP)** Project is a prospective static group comparison design study to determine the feasibility of implementation in a primary health centres in Belagavi, India. Process outcomes will include success with recruitment, participant retention and ability to collect outcome measures. Clinical outcomes will incorporate measures of parenting behaviours to explore the potential impact of SDP on positive parenting outcomes and to identify factors affecting feasibility and acceptability of a brief parent-directed intervention in Belagavi, India.

Breastfeeding Education Support

“**Breastfeeding Education Support Tool for Baby (BEST4Baby)**” an upcoming project funded by Fogarty International Center, National Institutes of Health, USA will utilize exploratory research and

community involvement to design and integrate mobile technology, culturally-appropriate breastfeeding education, and a community-based approach to increase breastfeeding support to mothers. The initiative will provide evidence that the BEST4Baby approach can achieve the public health objective of improving rates of exclusive breastfeeding for 6 months and continued breastfeeding for an appropriate time thereafter.

In 2011, the World Health Organization released the Guidelines on Optimal Feeding for Low Birthweight Infants in Low-and Middle-Income Countries (LMICs). However, 70% of the guidelines are based on “low or very low” quality of evidence, and the majority of research regarding mother’s own milk alternatives has been in high-income, hospital-based settings. There is a pressing lack of information about LBW infants in LMICs: existing feeding patterns; rates and causes of unsuccessful breastfeeding; and effective options for feeding, fortification, or supplementation with micronutrients. Forty global health organizations recently issued an urgent call to action to improve the evidence base, specifically for neonatal care units. **Low-birthweight Infant Feeding Exploration study (LIFE)** hopes to address these gaps with the overall study goal as to understand feeding options for LBW infants in LMIC settings, including current feeding practices, health outcomes, and potential interventions. The study is being implemented in four study sites located in three countries: Tanzania, Malawi, and India. JNMC Belagavi, JJMMC Davanagere, SSIMSRC Davanagere and SCB Medical College Cuttack are the sites in India.

Health System Intervention

“Evaluation of an Emergency Obstetrics and Newborn Care Intervention Package to Reduce Adverse Pregnancy Outcomes in Low Resource Settings (The EmONC Trial)” tested an integrated package of strategies for improving pregnancy outcomes. The strategies included creating awareness in the communities for birth planning and hospital transport, birth attendant training for early recognition of pregnancy and newborn complications, and hospital staff training in the management of obstetric and neonatal emergencies. Lessons learnt from this project suggest that achieving improvement in pregnancy outcomes in these settings will require substantially more obstetric and newborn care infrastructure and provider training and community mobilization alone will not be sufficient.

‘Implementation of the WHO Safe Childbirth Checklist program’, a novel childbirth safety program for institutional births incorporating a 29-item checklist containing essential practices that target the major causes of childbirth-related mortality, was evaluated as a pilot, pre-post-intervention study in a sub-district level birth centre in Karnataka, India between July and December 2010 by JNMC Research Unit with a Collaborative effort with the World Health Organization and Harvard School of Public Health. The study demonstrated a significant improvement in the delivery of 28 out of 29 essential safety practices by health workers. This validation of the WHO Safe Childbirth Check List Program has resulted inclusion as one of the component in ‘Maternal and Newborn Health Tool Kit’ by the Ministry of Health& Family Welfare, Government of India.

Using WHO Safe Childbirth Checklist, as a quality improvement tool, a matched-pair, cluster randomized controlled trial was conducted in 60 pairs of facilities across 24 districts of Uttar Pradesh, India to test the effect of **‘Better Birth program’**, an 8-month coaching-based implementation of Safe Childbirth Checklist, on a composite outcome of perinatal death, maternal death and maternal severe complications within 7 days after delivery. Outcomes assessed on 8 to 42 days after delivery were

compared between the intervention and control groups. JNMC Research Unit investigators provided the technical consultation for the implementation of this study.

JNMC Research Unit was involved in the conduct of a pilot study of an **“Indicator to Measure Intrapartum Stillbirth and Immediate Neonatal Death”** conducted among pregnant women admitted to 6 study hospitals in 4 low-income countries viz. India, Pakistan, Kenya and Democratic Republic of Congo, funded by National Institute of Child Health and Human Development and Engender Health and Maternal Health Task Force, USA from June 2011 to 2012. Foetal Heart Sounds were monitored using a specialized Sonoline B Foetal Doppler (DOPTONE). The results demonstrated the possibility of accurately determining the foetal viability on admission using this simple instrument which might form the basis of a low-cost sustainable program to monitor and evaluate efforts to improve the quality of care and thereby reducing the in-hospital perinatal mortality in low-income countries.

Despite decades of sustained investment, 300,000 women and 3 million newborns continue to die each year in the days surrounding childbirth. While there are many reasons for these unacceptable statistics, chief among them is a stubborn lack of progress in the development of new diagnostic and risk-stratification strategies appropriate for resource-poor settings. Indeed, most of the lab tests, monitoring technologies, drugs, and clinical approaches currently available for pregnancy care in the global south have not changed in 50 years. **Limiting Adverse Birth Outcomes in Resource-Limited Settings Prospective, Observational Cohort (LABOR) study** is planned to exhaustively document the course and outcomes of labor, delivery, and the immediate postpartum period in settings where the occurrence of adverse birth outcomes is high. The study also aims to create the largest, most carefully documented observational cohort of labor and delivery ever assembled in the developing world. The goal is to precisely characterize the incidence of adverse labor outcomes and their measurable antecedents in diverse populations while carefully documenting patterns of care. Newer tools will be utilized in low-resource healthcare facilities for better risk stratification and earlier diagnosis to improve intrapartum outcomes. This study is to be conducted in Belagavi, Karnataka and Balasore, Odisha with the funding from the Bill and Melinda Gates Foundation.

The Partograph is an important clinical tool for monitoring a woman’s progress during labour and childbirth that is in routine use worldwide. A revised version of the WHO Partograph – the **“WHO Labour Care Guide (LCG)”** – has been developed to make it easier for healthcare providers to routinely implement WHO’s latest evidence-based recommendations on intrapartum care. **Evaluating the WHO Labour Care Guide in clinical settings study** aims to evaluate the usability, feasibility and acceptability of the LCG, and to explore barriers and facilitators to its use by healthcare providers in clinical settings. The study is being conducted in Belagavi, Karnataka and Balasore, Odisha.

Visit of US Health Secretary to JNMC Research Unit

Ms. Kathleen Sebelius, Secretary of Health, heading the department of Health and Human Services of the USA visited J N Medical College, Belagavi on **15th January, 2012** to observe the research activities conducted at the village level. Congratulating the JNMC research team for the outcomes in the community based studies focused on women's and children's health, she lauded J. N. Medical College for its commitment to improve the health status of rural India. On this occasion, she lauded the leadership of Dr Prabhakar Kore and his encouragement to community based research for the benefit of rural women and children and invited the team to participate in a meeting of the Global Network in Washington held in June 2012. Acknowledging the outstanding research contribution of the

research team, she reaffirmed the continued support of US Government for the next five years through 2018.

Dissemination to the Stakeholders and Scaling up of the Activities

International PPH Congress – 2006

Women's and Children's Health Research unit of J N Medical College organized the International Congress on Evidence Based Interventions to Prevent Post-partum haemorrhage: Translating Research into Practice at Park Hyatt, Utorda, Goa from 12th to 15th July, 2006 to disseminate the Oral Misoprostol Trial conducted at JNMC between 2001 – 2006. Dr R.D.Pandit, Past President and Editor Emeritus, FOGSI, Mumbai was the chief guest and inaugurated the congress. 138 delegates from India, USA, Pakistan, Nepal, Bangladesh and Cambodia attended the congress.

PPH Congress – 2014

A PPH Congress was organised at Goa on 3rd and 4th September, 2014 to disseminate the results of another major trial – 'Two community strategies comparing use of misoprostol for early treatment/secondary prevention to primary prevention for postpartum haemorrhage: a randomized cluster non-inferiority study in Bijapur district, Karnataka, India' in collaboration with Gynuity Health Projects, New York, USA and University of Illinois at Chicago, and University of California at San Francisco with funding from Bill & Melinda Gates Foundation, USA

National Seminar on Interventions for Reducing Maternal and Newborn Mortality – 2014

Women's and Children's Health Research unit of J N Medical College organized the **National Seminar on "Interventions for Reducing Maternal and Newborn Mortality: Translating Research Evidence to Practice"** on 5th & 6th of September 2014. Chief Guest Dr. Sharanprakash Patil, Honourable Minister of State for Medical Education, Government of Karnataka inaugurated the event. The seminar provided an overview of the completed and on-going research projects with a main focus on Helping Babies Breathe Project. The key focus of the seminar was to share with various stakeholders – academicians, policy makers, representatives of national and international agencies working in the area of MNCH research, officials of the Ministry of Health – the evidence emanating from the research studies implemented by the research unit in Belagavi, Bagalkote and Bijapur (Vijayapura) districts.

International Conference on Maternal and Newborn Health Research - 2016

To commemorate the Centenary of KLE Society (1916 - 2016), the JNMC Women's and Children's Health Research Unit, Belagavi organized the International Conference on Maternal and Newborn Health Research on 5th & 6th of March 2016. This conference witnessed the participation of nearly **400** delegates (364 national and 26 international delegates) and 30 resource persons from 14 countries including Argentina, USA, Canada, United Kingdom, Switzerland, Egypt, Kenya, Uganda, Nigeria, South Africa, Pakistan, Singapore and Thailand. This platform brought together leading experts from around the world to debate priority research areas besides providing evidence from a number of completed and ongoing research projects focused on reducing maternal and newborn mortality/morbidity from Postpartum Haemorrhage, Hypertensive Disorders of Pregnancy, Birth Asphyxia and Preterm Birth. It also provided an opportunity to review the regulatory environment pertaining to the conduct of clinical research. The key focus of the conference was to share with various stakeholders – academicians, policy makers, representatives of national and international agencies working in the

area of MNCH research, officials of the Ministry of Health – the evidence emanating from the research studies implemented by the research unit in Belagavi, Bagalkot and Bijapur districts. **34** International and National Experts delivered guest lectures followed by interactive sessions.

2nd International Conference on Maternal and Newborn Health - 2018

The JNMC Women's and Children's Health Research Unit, KAHER's J N Medical College, Belagavi hosted the 2nd International Conference on Maternal and Newborn Health on 26th & 27th of March 2018 to share the results of some recently concluded research studies viz., CLIP Study, Clindamycin Trial & Women First Trial to reduce Maternal and Newborn mortality and morbidity and initiate a dialogue with the key stakeholders including academic research community, program managers and policy makers, both nationally and globally. This conference brought together leading experts in the areas of maternal and newborn health from around the world to discuss future priority research areas. A total of 60 International delegates representing 22 Nationalities USA, UK, Canada, Denmark, Australia, etc. and 240 National delegates including the Obstetricians and Gynecologists, Pediatricians, Public Health Experts, Nutritionists, participated in this event.

The conference was inaugurated by Dr Harsh Vardhan, Hon'ble Union Minister of Science & Technology; Earth Sciences; and Environment, Forest and Climate Change, Government of India. Honorable Chairman, KLE Society & Member of Parliament of Rajya Sabha, Dr. Prabhakar Kore presided over the program. Dr Mark Tykocinski, Executive Vice President for Academic Affairs, Thomas Jefferson University and Dr. Tonse N K Raju, Chief of Pregnancy & Perinatology, NICHD, USA were the guests of honour. Representatives from WHO, NICHD, NIH, Bill & Melinda Gates foundation, ICMR, National Institute of Nutrition, members of KLE Society and various research scholars attended the conference. The conference comprised of Scientific Deliberations, Key Note Addresses and Panel Discussion on current issues in maternal and newborn health viz. Post-partum haemorrhage, Hypertensive disorders of pregnancy, Maternal Nutrition and Preterm Birth. This conference provided a platform to set new guidelines to improve maternal and newborn health.

WHO - CHAMPION TRIAL: Steering Committee Meetings at J. N. Medical College, Belagavi

The JNMC Women's and Children's Health Research Unit hosted the WHO – CHAMPION Trial Steering Committee Meeting at the JNMC Campus on 7th and 8th March, 2016. Delegates from 13 Countries viz. USA, UK, South Africa, Denmark, France, Nigeria, Brazil, Switzerland, Egypt, Kenya, Pakistan, Thailand, Uganda and from India, delegates from four participant states Maharashtra, Uttar Pradesh, Odisha and Karnataka participated in the meeting. Similarly, JNMC hosted a similar Steering Committee Meeting on 28th and 29th March, 2018. A total of 25 delegates from 12 countries participated in the meeting.

WHO Collaborating Center for Research in Maternal and Perinatal Health

Women's and Children's Health Research Unit, Jawaharlal Nehru Medical College, KLE Academy of Higher Education and Research, Belagavi is designated as a "WHO Collaborating Center for Research in Maternal and Perinatal Health" for a period of four years effective from September 16, 2019.

Faculty:

- Dr Shivaprasad S Goudar, Professor of Physiology & Research Coordinator – **Center Head**

- Dr Sangappa M Dhaded, Professor of Pediatrics
- Dr Yeshita V Pujar, Professor of Obstetrics and Gynecology
- Dr Manjunath S Somannavar, Associate Professor of Biochemistry
- Dr Sunil S Vernekar, Associate Professor of Physiology
- Dr Yogesh Kumar S, Associate Professor of Community Medicine
- Dr Avinash Kavi, Assistant Professor of Community Medicine

Terms of Reference:

1. In alignment with WHO goals, to provide capacity building through Research Methodology Workshops at country level.
2. To participate in collaborative research in the area of Maternal and Newborn Health developed under WHO's leadership.
3. As agreed with WHO, disseminate and scale up evidence based interventions in the area of Maternal and Newborn Health.

The center will work in the subject areas of:

1. Reproductive health (excluding HIV/AIDS);
2. Health promotion & education; AND
3. Child & maternal health.

The types of activity to be conducted by the center are:

1. Research;
2. Information dissemination; AND
3. Training and education

Highlights:

Globally there are **825** WHO Collaborating Centers, of which currently India has **56** active Centers.

Among these 56 currently active Indian WHO CCs, JNMC Research Unit is ONE of ONLY seven in the private sector (others being - Dr Mohan's Diabetes Hospital, Chennai; LV Prasad Hospital, Hyderabad; CMC, Vellore; SRM, Chennai; and Arvind Hospital, Madurai).

Among the FOUR WHO CCs in Karnataka, (NIMHANS – 2 centers, National Tuberculosis Institute) JNMC Research Unit is the ONLY ONE in the private sector.

COLLABORATIONS

The Research Unit has research collaborations with the following international and national funding agencies, universities and institutions:

Sponsors: Governmental Agencies

- World Health Organization, Geneva, Switzerland
- National Institute of Health and Human Development, NIH, Bethesda, MD, USA
- National Institute of Neurological Diseases and Stroke, NIH, Bethesda, MD, USA
- Fogarty International Center, Bethesda, MD, USA
- National Cancer Institute, National Institutes of Health, Bethesda, MD, USA

- USAID, Washington, USA
- Medical Research Council, UK
- NORAD, Norway
- International Atomic Energy Agency, Vienna, Austria
- Indian Council of Medical Research, New Delhi, India
- Department of Biotechnology, Govt. of India

Sponsors: Foundations/NGOs

- Bill & Melinda Gates Foundation, USA
- Thrasher Research Fund, USA
- Merck for Mothers, USA
- Children's Investment Fund Foundation, UK

Collaborators

International: Universities

- University of Illinois at Chicago, Chicago, USA
- University of Missouri at Kansas City, Kansas City, USA
- University of Alabama at Birmingham, Birmingham, USA
- University of Colorado Health Sciences Center, Denver, USA
- University of California, San Francisco, USA
- Columbia University, New York, USA
- University of North Carolina at Chapel Hill, USA
- Harvard T. H. Chan School of Public Health, Boston, USA
- John's Hopkins Bloomberg School of Public Health, Baltimore, USA
- Christiana Care Health System, Wilmington, DE, USA
- Thomas Jefferson University, Philadelphia, USA
- Vanderbilt University, Nashville, TN, USA
- University of British Columbia, Canada
- King's College, London, UK
- The University of Sheffield, UK
- University of Zambia, Lusaka, Zambia
- University of Pretoria, Pretoria, South Africa

International: Research Institutes

- RTI International, North Carolina, USA
- Gynuity Health Projects, New York, USA
- Program for Appropriate Technologies for Health (PATH), Seattle, USA

National: National Medical Colleges/Universities

- B.V.V.S.'s S. N. Medical College, Bagalkot, Karnataka
- BLDE University's Shri B. M. Patil Medical College, Vijayapura, Karnataka
- J. J. M. Medical College, Davanagere, Karnataka

- S S Institute of Medical Sciences and Research Center, Davanagere, Karnataka
- Karnataka Institute of Medical Sciences (KIMS), Hubballi, Karnataka
- Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh
- S. C. B. Medical College, Cuttack, Odisha
- Fakir Mohan Medical College & Hospital, Balasore, Odisha
- Government Medical College, Nagpur, Maharashtra
- Sawai Man Singh Medical College, Jaipur, Rajasthan

National: Research Institutes

- Regional Medical Research Centre - National Institute of Traditional Medicine (NITM), ICMR, Belagavi,
- National AIDS Research Institute, Pune, India
- Lata Medical Research Foundation, Nagpur, Maharashtra
- The Karnatak Cancer Therapy And Research Institute (KCTRI), Hubballi, Karnataka
- Model Rural Health Research Unit (MRHRU), Sirwar, Raichur, Karnataka