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DISCOVERING LINKS BETWEEN FOOD TIMING AND METABOLIC HEALTH

Studying data from 1,300 pregnant women and young children, KKH researchers uncover implications on metabolic health associated with predominantly night-time caloric intake.



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MICA MCI (P) 095/11/2017 REG NO 198904227G

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Discovering links between food timing and metabolic health

Studying day-night caloric intake, fasting intervals and eating episodes in pregnant women and infants has led to the discovery of implications on metabolic health associated with predominantly night-time caloric intake. This may be a modifiable risk factor against future health problems.

Dr Loy See Ling



Research into nutrition has traditionally focused on the quantity and quality of food ingested, linking portion size, energy and nutrient composition with metabolic outcomes. However, there is mounting evidence that the time profile of food intake is metabolically relevant above and beyond food portion and composition. The timing of when we eat has been documented as an important determinant of circadian rhythms in metabolic pathways.

In animal models, nocturnal rodents given eight to 12 hours of food access during their active phase (i.e. night-time) had improved oscillations of circadian clock components in the liver and glucose tolerance, compared to rodents fed under an *ad libitum* regimen. In clinical trials among the adult human population, enhanced weight loss and improved glycaemic control were found in those with lower caloric intake in the evening than morning, despite similar total caloric intake for the entire day.

On the basis of these studies, it was concluded that predominantly night-time caloric intake could negatively impact glucose and metabolic regulations. To date, this area remains largely unknown among pregnant women, a high-risk population vulnerable to gestational hyperglycaemia; as well as among young children, where early childhood serves as a critical window for obesity and metabolic disease prevention.

A better understanding of how the timing of food intake, fasting intervals and eating episodes relates to plasma glucose concentrations in pregnant women and weight status in young children may lead to improved strategies in managing metabolic health among these target populations.

CLOSE LINKS BETWEEN MATERNAL AND CHILD FOOD TIMING, AND METABOLIC HEALTH

Leveraging Singapore's ideal conditions for conducting circadian-related studies, where

sunlight exposure occurs at a fairly constant length of 12 hours daily throughout the year (i.e. sunrise is approximately at 7.00am and sunset is approximately at 7.00pm), we conducted several studies examining the daytime and night-time food intake of pregnant women and 12-month-old infants.

We studied the time profile of food intake from the aspects of day-night caloric intake, fasting intervals and eating episodes – looking for associations with plasma glucose concentrations and weight status, respectively.

Data from Growing Up in Singapore Towards healthy Outcomes (GUSTO), a large scale mother-offspring cohort study, was used and the studies were led by Dr Loy See Ling, Research Fellow, Department of Reproductive Medicine; Associate Professor Fabian Yap, Head and Senior Consultant, Endocrinology Service; and Associate Professor Jerry Chan, Senior Consultant, Department of Reproductive Medicine, from KK Women's and Children's Hospital.

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IMPLICATIONS OF PREDOMINANTLY NIGHT-TIME CALORIC INTAKE FOR PREGNANT WOMEN

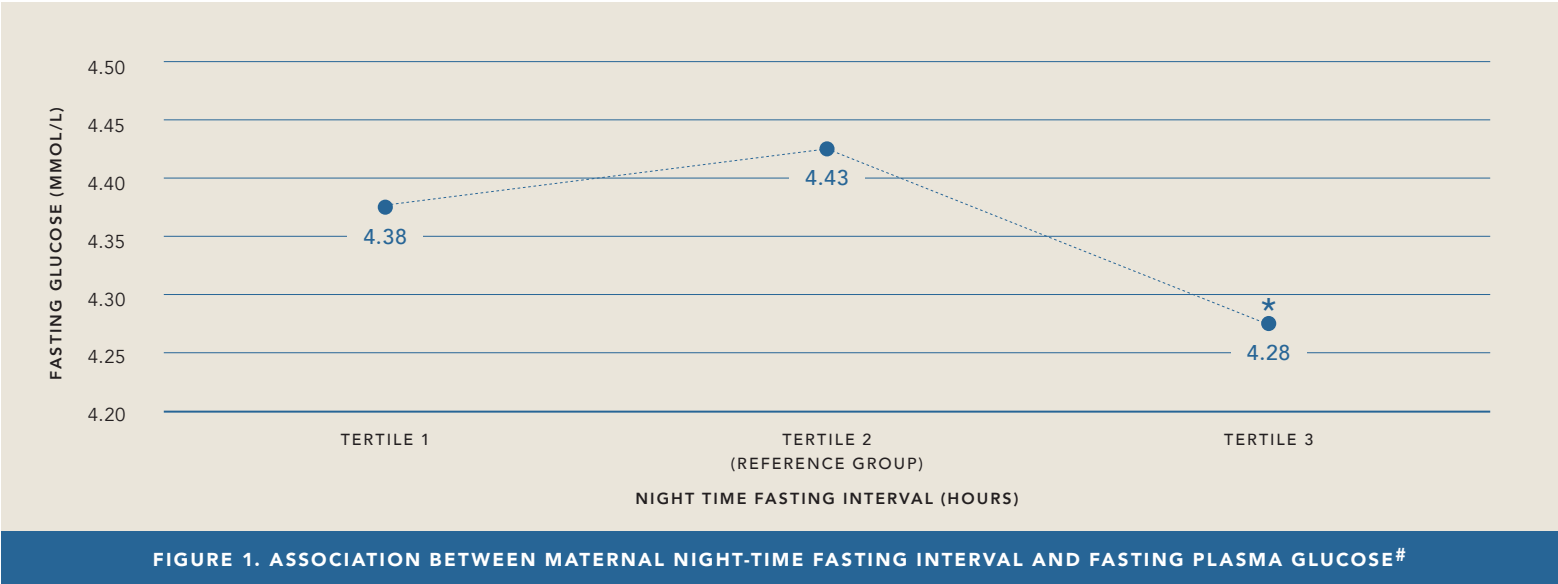
Among 985 pregnant women, it was found that 15 per cent consumed 50 per cent more calories during night-time (from 7.00pm to 6.59am) than daytime (from 7.00am to 6.59pm) at 24 to 28 weeks' gestation¹. Pregnant women with a greater night-time caloric intake had higher levels of fasting plasma glucose during the late-second trimester¹.

It was subsequently demonstrated that pregnant women with longer night-time fasting intervals had lower levels of fasting plasma glucose (Figure 1)². Furthermore, pregnant women with fewer daily eating episodes were found to have reduced levels of two-hour plasma glucose (Figure 2)².

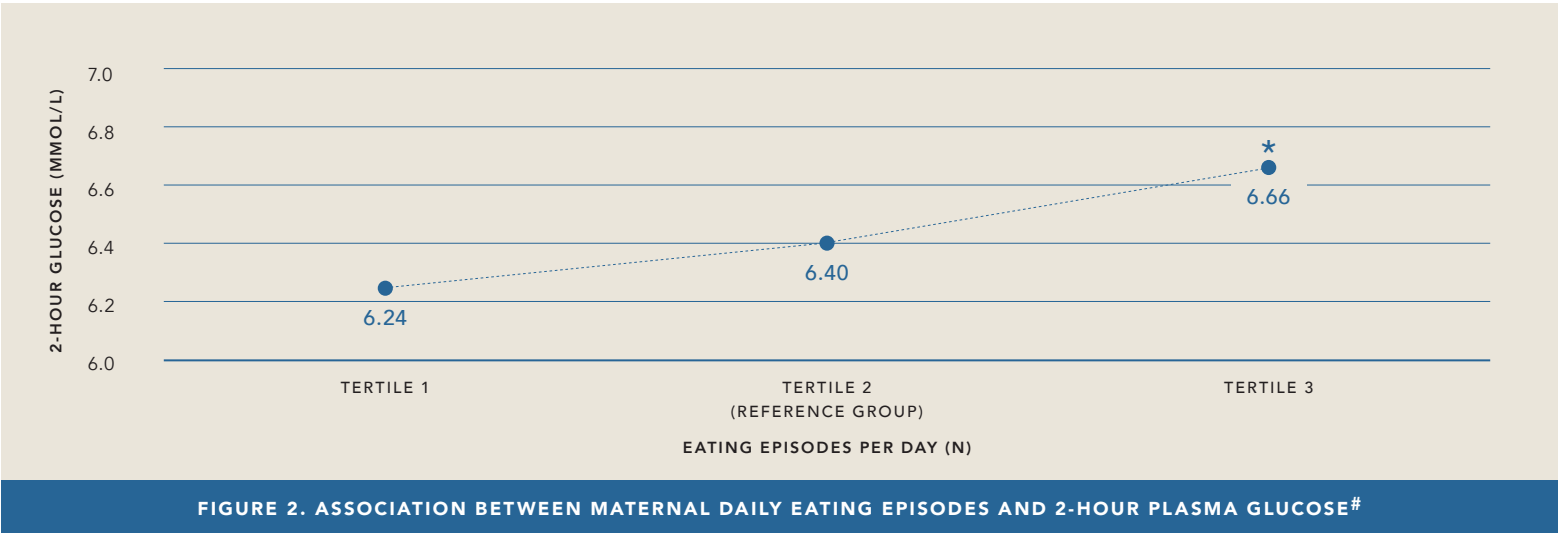
While these changes in glycaemic levels in response to food timing may seem inconsequential, however, over time, they may have a significant effect to aid prevention of gestational hyperglycaemia and its consequences for the mother/offspring in view

that the risks of adverse perinatal outcomes can occur, which increase continuously in association with rising maternal glucose levels.

Gestational hyperglycaemia contributes to adverse perinatal outcomes, neonatal adiposity and long-term risk of obesity in offspring. These occur throughout the range of glycaemia, even at concentrations below the diagnostic cut-off for gestational diabetes mellitus. Evidence suggests that even modest glycaemic improvement in pregnant women with mild glucose intolerance improves perinatal outcomes².



*p<0.05, significantly different from the reference group at tertile 2.



*p<0.05, significantly different from the reference group at tertile 2.

#Data were presented as mean, and adjusted for maternal age, ethnicity, education, employment status, night-shift status, parity, body mass index, physical activity, sleep duration, bedtime, total energy intake, and percentage of energy at night.

IMPLICATIONS OF
PREDOMINANTLY NIGHT-TIME
CALORIC INTAKE FOR INFANTS

At 12 months, an infant’s daily sleep/wake cycle is moderately stabilised with an increasing consolidation of sleep during the night compared with early infancy, implying that consistent and stable daily feeding practices may be in place. Hence, infant feeding practices at 12 months deserve more attention, as this is a transition period that is critical in setting the foundation for food choices and eating habits later in life.

Among 349 12-month-old infants, it was found that 19 per cent were predominantly night-time feeders – consuming 50 per cent more calories during the night (from 7.00pm

to 6.59am) than in the day (from 7.00am to 6.59pm). These infants had a larger weight gain from 12 to 24 months and higher risk of becoming overweight at 24 months than infants who were predominantly fed during daytime hours.

These findings suggest that consuming larger quantities of energy predominantly during the night-time may be metabolically disadvantageous, even from the age of 12 months, and may be a modifiable risk factor against future health problems³.

INFLUENCING FOOD TIMING TO
IMPROVE HEALTH OUTCOMES

These findings raise the possibility of including advice for pregnant women and

caregivers of young children on adopting time-based eating patterns to improve their long-term metabolic health. Benefits for pregnant women can include enhanced glucose level control and a lower risk of gestational hyperglycaemia.

Benefits for young children can include the establishment of feeding behaviours that may habituate the child to maintain similar eating patterns in adulthood – making early childhood a potentially critical window for obesity prevention.

These findings may also be valuable to inform the custom of night-time eating that is commonly practised in modern society, towards bettering public health.

To confirm our findings and evaluate the clinical practice applicability, more long-term and large-scale randomised trials are warranted.

Preliminary findings from observational studies are promising, and work is ongoing to analyse long-term weight outcomes for young children in relation to their day-night feeding patterns.

These studies are supported by the Singapore National Research Foundation under its Translational and Clinical Research (TCR) Flagship Programme and administered by the Singapore Ministry of Health’s National Medical Research Council (NMRC), Singapore (NMRC/TCR/004-NUS/2008; NMRC/TCR/012-NUHS/2014).

Additional funding is provided by the Singapore Institute for Clinical Sciences, Agency for Science Technology and Research (A*STAR), Singapore.

KEY RESEARCH FINDINGS FOR WOMEN:
1. Among 985 pregnant women, 15% consumed 50% more calories during the night than in the day at 24-28 weeks’ gestation ¹ .
2. Pregnant women with greater night-time caloric intake had higher fasting plasma glucose at late-second trimester ¹ .
3. Pregnant women with longer night-time fasting interval had lower fasting plasma glucose ² . Those with fewer daily eating episodes were found to have reduced levels of two-hour plasma glucose ² .

KEY RESEARCH FINDINGS FOR CHILDREN:
1. Among 349 12-month-old infants, 19% consumed 50% more calories during the night than in the day ³ .
2. The feeding of infants predominantly during the night was associated with weight gain and risk of overweight in early childhood ³ .
3. Consuming larger quantities of energy predominantly during the night may be metabolically disadvantageous, even from the age of 12 months, and may be a modifiable risk factor against future health problems ³ .

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Dr Loy See Ling, Research Fellow, Department of Reproductive Medicine, KK Women’s and Children’s Hospital

Dr Loy See Ling completed her Bachelor of Science (Dietetics) and Doctor of Philosophy (Human Nutrition) in Malaysia. She is currently conducting research related to maternal and child health by engaging in preconception and pregnancy prospective cohort studies in Singapore – namely the ‘Growing Up in Singapore Towards healthy Outcomes’ (GUSTO) study and ‘Singapore PREconception Study of long-Term maternal and child Outcomes’ (S-PRESTO) study. Dr Loy has a special interest in early nutrition and its effects on later health, in particular obesity and diabetes.

How Do I Know It's Infantile Colic?

Recommendations for assessment, diagnosis and management for the clinical presentation of persistent crying and fussing in an infant.

Dr Nandhakumar Nagarajan



The clinical presentation of a young infant often crying for long hours and mostly in the evening, for reasons that may not be immediately apparent, is a common situation experienced by many primary healthcare providers.

Infantile colic, diagnosed according to the Rome IV criteria, is the clinical presentation of an infant who has cried or fussed for three or more hours a day, during three or more days in the preceding week – with the history confirmed by a 24-hour behaviour journal maintained by the caregiver¹. The caregiver will need to record the duration and frequency of crying, the infant's feeding pattern, bowel output and any other associated symptoms.

This behavioural phenomenon often presents in the first month of life, and continues until four to six months of age. While managing a crying infant can be a distressing routine for caregivers, fortunately, this behaviour generally starts to improve by the time weaning is introduced.

DETERMINING THE RIGHT CAUSE

The true incidence and prevalence of infantile colic can be challenging to estimate, as its aetiology is complex and ill-defined, and symptoms can be vague and non-specific. Further, varying diagnostic criteria are applied in different parts of the world, and parental perception of fussiness or abnormal crying can be subjective, influencing the eventual diagnosis.

The clinical phenomenon is thought to be caused by various factors which include altered gut motility, gastro-oesophageal reflux, milk protein allergy or intolerance, lactose intolerance or intestinal distension from increased bowel gas and altered intestinal microbiome^{2,3}.

In a small number of infants, this behaviour may be associated with more serious medical conditions such as intussusception, visceral pain, cerebral irritation from infections, or non-accidental injuries. In such cases, non-specific and excessive crying may be the only presenting symptom. The steps for assessment of infantile colic by community healthcare practitioners are outlined in Table 1.

TREATMENT AND INTERVENTION

In the absence of pathological concerns, infantile colic is self-limiting and has a good prognosis. In these instances, the condition can be effectively managed by providing caregivers with management advice, caring reassurance and regular follow-up for the infant.

While some caregivers may opt for over-the-counter formulations to soothe their crying babies, there is currently no strong scientific evidence to recommend their routine use in clinical practice.

The majority of young infants who present to the General Paediatrics Service at KK Women's and Children's Hospital with non-specific and excessive crying do not have serious medical problems.

However, should a potential underlying medical condition be identified, timely and appropriate referral for tertiary assessment and intervention is beneficial in managing the infant's condition, and minimising the distress experienced by both caregiver and child.

Table 2 outlines some of the common causes of infantile colic, their management recommendations and criteria for tertiary assessment.

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1. Judith Zeevenhooven, Ilan J.N. Koppen, and Marc A. Benninga. The New Rome IV Criteria for Functional Gastrointestinal Disorders in Infants and Toddlers. *Paediatric Gastroenterology, Hepatology & Nutrition* 2017 March 20(1):1-13
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TABLE 1. ASSESSMENT OF INFANTILE COLIC BY COMMUNITY HEALTHCARE PROFESSIONALS

STEP

01

HISTORY TAKING

- Gather information from caregivers on the history of the infant’s behaviour, and look out for symptoms that may suggest infantile colic, in accordance with the Rome IV criteria.

STEP

02

PHYSICAL EXAMINATION

- Assess the general wellbeing of the infant by checking the adequacy of growth parameters and conducting a normal systemic examination.

Red flags to look out for:

- Fever
- Bloody stool
- Distended abdomen, abdominal guarding, bilious vomiting and discolouration of the abdominal wall
- Altered mental state (e.g. drowsiness), poor feeding and/or not waking up for feeds, alternating with undue irritability and excessive crying
- Signs of non-accidental injury such as unexplained bruises, swelling of the scalp, and paucity of limb movements, associated with excessive crying while handling the infant

STEP

03

RECOMMENDATIONS

- If any of the above-mentioned red flags are observed, the infant should be promptly referred for tertiary assessment.
- If infantile colic is suspected, caregivers should be given reassurance, advice on appropriate feeding, and suggestions to minimise aerophagia through proper winding techniques.
- If caregivers are smokers, they should be advised to quit, as maternal smoking during pregnancy and in the post-partum period is a risk factor for infantile colic⁴.
- Breastfeeding should be encouraged, and advice provided on proper breastfeeding, as breast milk is easy to digest and can be emptied from the stomach quickly, which helps in lowering the incidence of gastro-oesophageal reflux, a common cause of infantile colic.
- Conduct medical reviews as necessary to monitor the infant's progress and provide parents with support.

STEP

04

FURTHER ASSESSMENT AND REFERRAL TO TERTIARY INSTITUTIONS

- If symptoms persist, conduct further examinations to identify other contributing medical conditions. Common medical conditions that present with infantile colic symptoms can include gastro-oesophageal reflux disease, cow’s milk protein intolerance, secondary lactose intolerance and constipation.
- If the infant is found to have a serious underlying medical condition, such as those characterised by the above-mentioned red flags, urgent referral should be made for tertiary assessment.

REFER A PATIENT

Polyclinics and community healthcare practitioners can contact KKH at **+65 6294 4050** to refer patients to the General Paediatrics Service for tertiary assessment and management for infantile colic.



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TABLE 2. RECOMMENDED MANAGEMENT FOR COMMON CAUSES OF INFANTILE COLIC

MEDICAL CONDITIONS	SYMPTOMS	ADVICE TO CAREGIVERS	MANAGEMENT	CRITERIA FOR REFERRAL TO SEEK TERTIARY ASSESSMENT
GASTRO-OESOPHAGEAL REFLUX	<ul style="list-style-type: none">• Infant regurgitates a large amount of milk• Poor growth• Weight loss	<ul style="list-style-type: none">• Minimise the occurrence of reflux by practicing anti-reflux positioning of the infant and careful winding after feeds• Avoid overfeeding	<ul style="list-style-type: none">• Treatment with medications such as ranitidine and domperidone can be considered following tertiary assessment.	<ul style="list-style-type: none">• Referral for tertiary treatment is recommended if the infant experiences failure to thrive, choking and aspiration due to reflux, and excessive distress and crying after feeds.
CONSTIPATION	<ul style="list-style-type: none">• Formed or harder stools, with reduced stool frequency	<ul style="list-style-type: none">• If fluid intake is inadequate, supplement milk feeds with water after the age of two to three months.	<ul style="list-style-type: none">• Treatment with medication such as glycerol suppositories and lactulose can be considered in infants under the age of six months following tertiary assessment. <i>Note: Lactulose can lead to increased flatulence, distension and peristalsis. Hence, dosages should be carefully calibrated for the infant's weight and age.</i>	<ul style="list-style-type: none">• Referral for tertiary assessment should be made if the infant passes hard or infrequent stools in spite of adequate hydration.
COW'S MILK PROTEIN INTOLERANCE	<ul style="list-style-type: none">• Family history of atopy• Infantile eczema• Gastrointestinal symptoms such as bloody stools and increasing stool frequency, which may suggest a milk protein allergy• Excessive gastro-oesophageal reflux	<ul style="list-style-type: none">• Exclusive breastfeeding can lessen the incidence of cow's milk protein intolerance, and can improve the infant's gut flora and facilitate mother-infant bonding.• Maternal dietary manipulation should be addressed only after tertiary assessment.	<ul style="list-style-type: none">• Assessment by a specialist is necessary to ascertain the possibility of this diagnosis. In suspected cases, the infant can be placed on a trial of hypoallergenic milk formula for two-to-four weeks to confirm the diagnosis.• Once diagnosis is confirmed, tertiary management of the condition is recommended.	<ul style="list-style-type: none">• Referral for tertiary assessment should be made as soon as the infant begins exhibiting symptoms suggestive of milk protein allergy.
SECONDARY LACTOSE INTOLERANCE	<ul style="list-style-type: none">• Often follows an episode of gastroenteritis, where the infant continues to have frequent liquid stools with explosive bowel movements and perianal excoriation• Secondary lactose intolerance is suspected if diarrhoeal symptoms persist for more than two weeks	<ul style="list-style-type: none">• Promote breastfeeding• Breastfeeding mothers are advised to let the infant first empty one breast before moving to the other one. This enables the infant to consume more hind milk, which has more water and less solute load. Foremilk contains more lactose, which may cause discomfort in infants with this condition.• Breastfeeding mothers should continue with their normal dietary practices; it is not advisable to refrain from dairy products.	<ul style="list-style-type: none">• This is a transient phenomenon that often improves with time. If the infant is breastfed, it is recommended to continue with breastfeeding.• If the infant is formula-fed, in the first week of diarrhoeal illness, it is not advisable to change to a lactose-free formula, as lactose has many beneficial properties. In the second week, the same formula can be continued if the frequency of the infant's stools is improving. If diarrhoeal symptoms persist for more than two weeks, a lactose-free formula can be trialled for two-to-four weeks.	<ul style="list-style-type: none">• Referral for tertiary assessment should be made if diarrhoea persists for more than two weeks, to assess the infant for lactose intolerance and provide guidance with dietary intervention.



Dr Nandhakumar Nagarajan, Head and Senior Consultant, General Paediatrics Service, KK Women's and Children's Hospital

With 20 years of experience in general paediatrics, Dr Nandhakumar Nagarajan began his career in India and underwent specialist training in the United Kingdom, where he later worked as a consultant paediatrician with the National Health System. Dr Nagarajan is currently Associate Program Director of the SingHealth Post Graduate Year 1 Program for KKH, and oversees the training needs of paediatric medicine residents, medical students and trainees.

Managing The High-Risk Pregnancy

Dr Lionel Karuna Mary, Dr Shephali Tagore and Dr Ann Wright

Every woman hopes for an uneventful pregnancy. However, in a small proportion of pregnant women who present for antenatal care – generally 10 to 20 per cent – their pregnancy and/or delivery is considered “high risk” due to their medical or obstetric history, or conditions relating to the pregnancy or fetus.

A high-risk pregnancy or delivery is defined as any condition which increases the likelihood of an adverse outcome for the expectant mother, fetus, or both. Such conditions are often complex, requiring detailed multidisciplinary planning, preparation and coordination leading up to, during and even after delivery.

As the largest tertiary referral hospital specialising in healthcare for women and children in Singapore, KK Women’s and Children’s Hospital (KKH) manages about 12,000 deliveries each year, of which approximately five per cent are patients with high-risk pregnancies who have been referred from other healthcare centres.

Management for high-risk pregnancies at KKH is coordinated by the Obstetric High Risk Clinic (OHRC), also known as the Complicated Pregnancy Clinic. In recent years, the number of patients attending the OHRC has risen from around 300 in 2014 to more than 1,000 in 2017.

Led by experienced obstetricians from the Department of Maternal Fetal Medicine at KKH, the OHRC coordinates multidisciplinary care with teams comprising obstetric physicians, neonatologists, anaesthetists, radiologists, geneticists, paediatric cardiologists and surgeons, and operating theatre staff to provide holistic management for the wide range of conditions and critical considerations associated with the high-risk pregnancy. An overview of conditions seen at the OHRC is as follows:

TABLE 1: OVERVIEW OF CONDITIONS SEEN AT THE OBSTETRIC HIGH RISK CLINIC (OHRC)

MATERNAL CONDITIONS	FETAL CONDITIONS	SPECIFIC PREGNANCY-RELATED CONDITIONS
<p>Maternal conditions constitute about 60 – 70% of cases seen at the OHRC, and include:</p> <ul style="list-style-type: none"> • Pre-existing medical conditions which may be affected by the pregnancy and for which the mother needs extra surveillance, review of medications and planning for delivery. These can include hypertension, gestational diabetes mellitus (GDM), auto-immune conditions, malignancies and infections. • Past obstetric history of potentially recurrent obstetric complications, such as, pre-eclampsia, GDM, and severe prematurity. • New onset obstetric conditions, such as, hypertensive disorders and GDM. 	<p>Fetal conditions constitute about 20% of cases seen at the OHRC, and include:</p> <ul style="list-style-type: none"> • Previous intra-uterine fetal loss • Genetic or structural fetal abnormalities in the previous or current pregnancy • Severe intra-uterine growth restriction • Multiple pregnancies 	<p>Specific pregnancy-related conditions constitute about 15 – 20% of cases seen at the OHRC, and include:</p> <ul style="list-style-type: none"> • Recurrent mid-trimester losses and possible cervical incompetence requiring a cervical cerclage • Suspected abnormally invasive placentation (i.e. placenta accreta or percreta) in women with previous uterine procedures or surgeries. <p>These rare conditions can be a cause of major maternal morbidity and even mortality, the risk of which can be reduced through meticulous pre-operative planning.</p>

THE OHRC ALSO PROVIDES:

1. Pre-pregnancy counselling

A vital aspect of favourable pregnancy outcomes for women with severe medical conditions is pre-conception / pre-pregnancy counselling and care, which aims to optimally control their conditions in conjunction with the medical team. These include patients with diabetes mellitus, epilepsy and thyroid diseases.

2. Postnatal counselling

Postnatal counselling often involves debriefing following a poor obstetric outcome – such as intra-uterine fetal death, stillbirth or an extremely premature delivery. These consultations enable discussion of perinatal events and results of investigations, follow-up of maternal conditions and the facilitation of transfer of care to relevant care teams. They are also an opportunity to make care plans for future pregnancy, if appropriate.

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CRITERIA FOR REFERRAL TO OHRC

For a number of reasons, high-risk pregnancies require careful planning and are ideally managed in the setting of an obstetric high risk clinic. Early recognition and referral allows adequate time for optimising care and planning delivery.

Decisions regarding the timing and mode of delivery are usually made during weekly multidisciplinary team meetings involving neonatologists and other specialists. Continuing surveillance of high-risk antenatal women is provided in the Obstetrics Day Assessment Centre and the Obstetric Monitoring Unit.

Patients may be directly referred to the OHRC from a number of sources including community healthcare practitioners such as family medicine clinics, polyclinics and general practitioners, or obstetricians and specialists from other disciplines whose patient is pregnant. The criteria for referral to OHRC are as follows:

TABLE 2: CRITERIA FOR REFERRAL TO THE OBSTETRIC HIGH RISK CLINIC (OHRC)*

**Consult the OHRC team for urgent referrals or when considering a referral*

CRITERIA	RECOMMENDED TIMEFRAME FOR REFERRAL TO OHRC
HYPERTENSIVE DISORDERS	
• Mild or moderate pre-eclampsia	1 – 2 weeks
• Chronic hypertension	2 weeks or earlier, if severe
• Severe pre-eclampsia with intra-uterine growth restriction or other complications such as GDM or diabetes mellitus	1 week or earlier
• Postnatal with eclampsia or intensive care unit stay in the most recent pregnancy	4 weeks
CERVICAL INCOMPETENCE	
• Past history of cervical incompetence or cerclage High risk of cervical incompetence due to other reasons such as cone biopsy	By 12 weeks' gestation
• Cervix dilated on scan or examination	Consult the OHRC team
• Short cervix on scan of less than 25mm and/or features of funnelling	1 – 2 weeks
• Post-cerclage follow up	1 – 2 weeks
MEDICAL / SURGICAL DISORDERS AFFECTING PREGNANCY	
• Thyroid disorders	2 weeks
• Cardiac disease	2 weeks
• Diabetes mellitus (pre-existing or abnormal results from an oral glucose tolerance test)	2 weeks
• Systemic lupus erythematosus, antiphospholipid syndrome and renal conditions	By 12 weeks' gestation
• Deep vein thrombosis or pulmonary embolism, and/or if patient is on anti-thrombotic medication	1 – 2 weeks
• Human immunodeficiency virus	1 – 2 weeks
• Cancers in pregnancy	1 – 2 weeks
• Pelvic mass or uterine malformations	2 weeks, depending on gestation
• Other medical or surgical conditions	Consult the OHRC team
FETAL COMPLICATIONS	
• Intra-uterine growth restriction (IUGR)	1 – 2 weeks if abnormal results are observed via a Doppler scan
• Other fetal anomalies or complications	Immediate referral to the KKH Fetal Medicine Clinic or Monochorionic Twin Clinic
• Complications in multi-fetal pregnancies	
COMPROMISED OUTCOMES IN A PREVIOUS PREGNANCY	
• Stillbirth/neonatal death	By 12 weeks' gestation
• Dehiscence/ruptured uterus	
• History of severe pre-eclampsia or eclampsia	
• Extremely preterm birth	
• Severe IUGR	
• Fetal anomaly	
• Other conditions that may affect maternal and fetal safe	
• Antenatal/postnatal visit	4 – 6 weeks
PLACENTA ACCRETA	
• Suspected or confirmed placenta accreta	Consult the OHRC team

CASE STUDY: EARLY MANAGEMENT OF CERVICAL INCOMPETENCE RESULTS IN SUCCESSFUL DELIVERY

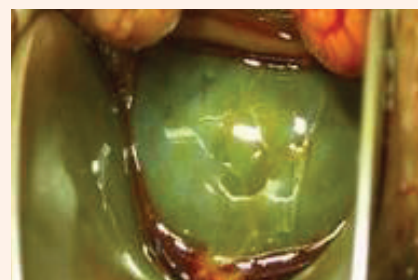
Twenty-nine-year-old Madam A had a history of cervical incompetence, causing her to experience miscarriages in her second trimester and having to place a cervical cerclage during previous pregnancies.

When she fell pregnant once more, Madam A presented to the Obstetrics High Risk Clinic at KKH at 15 weeks' gestation, and was offered cervical surveillance to manage her condition. During her antenatal check-up at 17 weeks, Madam A's cervical length was measured and found to be within the normal range. However, in view of her past history, she opted for a cervical cerclage to be placed electively at 18 weeks of gestation, which was subsequently removed at 34 weeks. After the removal, Madam A

developed some irregular tightening and, in the following week, she went into labour and delivered a healthy boy.

A cervical cerclage is a purse string suture, commonly placed at the cervico-vaginal junction to keep the cervix occluded. In selected groups of patients, cervical cerclage has shown to reduce the risk of mid-trimester pregnancy losses and early or extremely premature deliveries.

Madam A's case demonstrated the benefits of managing cervical incompetence at an early stage of pregnancy. Community healthcare practitioners and obstetricians can take note of the following signs in patients with cervical incompetence, which prompt for an early referral to a tertiary institution for follow up and management:



Before: Bulging membranes at the cervico-vaginal junction, indicating a prematurely dilated cervix.



After: A cervical cerclage in place at the cervico-vaginal junction to keep the cervix occluded.

CRITERIA FOR EARLY REFERRAL FOR CERVICAL INCOMPETENCE

MANAGEMENT OPTIONS

A history of one or more mid-trimester loss

Cervical surveillance

A cervix length of less than 25mm that is diagnosed through a scan, or evidence of the shortening of the cervix length

Cervical cerclage

Painless bleeding or discharge before 24 weeks of gestation, and a speculum examination indicating bulging membranes

Rescue cerclage can be attempted, with variable degree of success

REFER A PATIENT

Polyclinics, community healthcare practitioners and private obstetricians can contact KKH at **+65 6294 4050** to refer patients to the Complicated Pregnancy Clinic for consultation and tertiary evaluation and management for high-risk pregnancies.



Dr Lionel Karuna Mary, Staff Physician, Department of Maternal Fetal Medicine, KK Women's and Children's Hospital

As lead for the Obstetric Monitoring Unit at KKH, Dr Lionel Karuna Mary has been providing care to mothers with high-risk pregnancy or delivery in the Obstetrics High Risk Clinic since 2012. Dr Karuna Mary is a passionate member of the team at the Department of Maternal Fetal Medicine.



Dr Shephali Tagore, Head and Senior Consultant, Department of Maternal Fetal Medicine, KK Women's and Children's Hospital

Dr Shephali Tagore leads in high-risk obstetrics and operative obstetrics, and implements risk reduction strategies towards safer clinical care. Dr Tagore is also Director of the O&G International Medical Programme at KKH, and is actively involved in teaching, training and research activities. She has a passion for organising overseas training in obstetrics emergencies within Southeast Asia, and leads teams in teaching simple and safe obstetric practices to improve perinatal outcomes.



Dr Ann Wright, Consultant, Department of Maternal Fetal Medicine, KK Women's and Children's Hospital

Dr Ann Wright underwent training in the United Kingdom and has been a member of the Department of Maternal Fetal Medicine at KKH since 2014. Dr Wright has an interest in high-risk pregnancy and labour ward management.

Tubal Reversal – Still Relevant In An IVF Era?



By Dr Chua Ka-Hee and A/Prof Tan Heng Hao

Tubal ligation, a contraceptive procedure where a woman's fallopian tubes are surgically blocked or severed, is one of the most prevailing contraceptive options due to its high success rate (more than 99%). Women who desire more children after undergoing tubal ligation can consider two options to achieve pregnancy: in-vitro fertilisation (IVF), or microsurgical reversal of ligation – which is also known as tubal reversal.

Tubal reversal is a delicate microsurgical procedure involving the excision of the scarred segment of a fallopian tube and the precise anastomosis (connection) of the healthy proximal and distal ends of the tube. As the fallopian tube has a very fine lumen, precise anastomosis is crucial for a successful outcome. Hence, medical professionals would require intensive training to acquire proficiency in this delicate procedure. The procedure can be done under laparoscopy, allowing rapid recovery and discharge from the hospital.

RESTORING NATURAL FERTILITY THROUGH TUBAL REVERSAL

In recent times, with improvements to IVF techniques and pregnancy outcomes, the role of tubal reversal in enabling pregnancy after ligation has come under scrutiny, with many patients and physicians preferring the IVF route.

However, KK Women's and Children's Hospital (KKH) has observed good results in patients who have undergone tubal reversal. The KKIVF Centre has seen up to 70 to 80 per cent chance of pregnancy in properly screened patients after undergoing tubal reversal through laparoscopy. As with all surgeries, tubal reversal is not without its risks, namely surgical risks and a higher risk of subsequent ectopic pregnancy.

Nonetheless, the main advantage of tubal reversal is that it allows women to have sustained chance of pregnancy with every menstrual cycle, compared to limited attempts with IVF.

Studies comparing these two methods have also shown tubal reversal to be significantly more effective in women less than 40 years of age¹. Hence tubal reversal is ideal for younger women with a reasonable chance of cumulative live births.

To optimise the chances of achieving pregnancy post-procedure, a couple requesting tubal reversal should have good natural fertility – preferably below the age of 40 years and with a healthy body mass index – the woman should have a good ovarian reserve, and the man should have a normal sperm count.

REFER A PATIENT

Polyclinics and community healthcare practitioners can contact KKH at **+65 6294 4050** to refer patients to the Reproductive Medicine Clinic for consultation and tertiary evaluation on their eligibility for tubal reversal.

References:

1. Tan HH, Loh SF. Microsurgical reversal of sterilisation - is this still clinically relevant today? *Ann Acad Med Singapore*. 2010 Jan; 39(1):22-6.

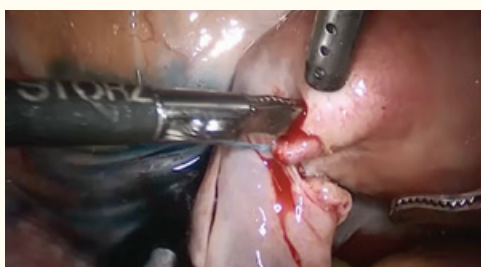
STEPS TO A TUBAL REVERSAL



Step 1. Beginning of a tubal reversal surgery, where a ligation clip causing separation of the fallopian tube into proximal and distal segments is located.



Step 2. Excision of the ligation clip.



Step 3. Blue dye is passed through the patent proximal segment of the fallopian tube.



Step 4. Stitches are placed at 12 o'clock of the fine tubal lumen.



Step 5. Anastomosis (connection) of the fallopian tube and lumen using sutures.



Step 6. End of the surgery, showing free flow of the blue dye from the fimbrial (distal) end to the proximal end of the fallopian tube, indicating that both ends of the fallopian tube are connected and the entire tube is patent.

CASE STUDY: A SECOND CHANCE AT PREGNANCY THROUGH TUBAL REVERSAL

Thirty-one-year-old Amy (not her real name) had undergone surgical sterilisation by ligation of her fallopian tubes after delivering her second child.

At the reproductive medicine clinic at KKH, Amy was presented with two choices to manage her subfertility – in-vitro fertilisation (IVF) or reversal of tubal ligation. She initially opted for IVF and underwent one IVF cycle, which turned out to be unsuccessful. Ten years later, she decided to try for a third child.

Subsequently, Amy decided to undergo a laparoscopic reversal of tubal ligation. During the operation, she was found to have signs of pelvic inflammatory disease: adhesions at the liver (Fitz-Hugh-Curtis syndrome) and around the tubes and ovaries. This caused further scarring and shortening of the fallopian tubes, on top of damage from the previous ligation. Despite this, the KKH surgeon was able to successfully reconstruct Amy's fallopian tubes.

Two months after the surgery, an ultrasound scan confirmed a healthy pregnancy. Amy is currently receiving antenatal care in KKH.

In this classic case study, IVF would have been instinctively the preferred choice for many, given the fact that pelvic inflammatory disease was present. In theory, the patient's fallopian tubes would have been damaged and unable to transport sperm and eggs effectively.

However, through laparoscopic reversal of tubal ligation, the medical team was able to treat the patient's pelvic inflammatory disease by excising adhesions and unhealthy portions of her fallopian tubes – successfully restoring the function of her fallopian tubes and enabling a pregnancy.



Dr Chua Ka-Hee, Associate Consultant, Division of Obstetrics and Gynaecology, KK Women's and Children's Hospital

Dr Chua Ka-Hee works closely with the Department of Reproductive Medicine at KKH, and has a subspecialty interest in male subfertility. Dr Chua is also a member of the Royal College of Obstetricians and Gynaecologists.



Associate Professor Tan Heng Hao, Head and Senior Consultant, Department of Reproductive Medicine, KK Women's and Children's Hospital

Associate Professor Tan Heng Hao is Head of the Department of Reproductive Medicine, and Deputy Chairman of the Division of Obstetrics and Gynaecology at KKH. He is also the Director of the KKIVF Centre and the National Sperm Bank. Passionate about education, A/Prof Tan is the Section Chair of Reproductive Medicine in the College of Obstetricians and Gynaecologists, Singapore, and was awarded the KK People Developer Award for Outstanding Clinical Teacher in 2013.

Opening New Doors To An Enhanced IVF Journey



Prof Ivy Ng, GCEO, SingHealth (far left, in yellow); Prof Alex Sia, CEO, KKH (far left, in white); Prof Kenneth Kwek, CEO, SGH (standing far right, in white); and A/Prof Tan Heng Hao, Director, KKIVF Centre, KKH (kneeling far right, in white) with the care team at the KKIVF@three laboratory.

Singapore's largest fertility centre – the KKIVF Centre at KK Women's and Children's Hospital (KKH) – has unveiled a new patient care and procedural wing to better cater to the growing number of patients seeking treatment with assisted reproductive techniques.

Completed in January 2018, the KKIVF@three facility is located on the third floor of the Children's Tower at KKH, and features a spacious recovery area, an oocyte pickup procedure room, embryo transfer rooms, and an enhanced IVF laboratory.

"Enhancing our hospital's physical spaces helps to create a warmer, more welcoming environment for patients, families and staff, as well as integrating enhanced technologies to benefit patient care," says Associate Professor Tan Heng Hao, Director, KKIVF Centre, and Head and Senior Consultant, Department of Reproductive Medicine, KKH.

"This is just the first step in ongoing enhancements to KKIVF facilities, as we continually look for better ways to provide holistic care for couples with a variety of medical conditions, and support them through exploring individualised treatments to help prepare them for pregnancy."

GIVING COUPLES THE BEST CHANCE FOR PREGNANCY

Established in 1993, the KKIVF Centre provides a holistic suite of services and treatment options to tackle the challenges that some couples may face while trying to conceive.

"Significant improvements have been made in the KKIVF laboratory culture environment," says A/Prof Tan. "This enables the centre to maintain formation rates of blastocysts (five-day-old embryos) of more than 70 per cent, a figure comparable to international standards."

"Leveraging on this, we have embarked on actively transferring a single blastocyst for selected patients to reduce the probability of multiple pregnancies – which are associated with higher risks for mother and baby – while improving implantation and pregnancy rates. Multiple pregnancy rates have since been on a positive downward trend."

Since 2017, the centre has maintained an Ovarian Hyperstimulation Syndrome (OHSS) incidence rate of less than one per cent – a five-fold drop compared to historical figures. This is achieved by early assessments and prompt treatments of patients who are suspected to be at risk, or already have early signs of OHSS. The debilitating medical condition occurs when too many ovarian follicles develop in response to medications.

To augment support for couples with complex subfertility issues, KKH also runs the first Recurrent Pregnancy Loss Clinic in Singapore which is staffed by specialists in reproductive medicine.

This allows patients to be cared for by specialists experienced in managing subfertility, with the capacity to refer patients for additional help from medical social workers, psychologists, immunologists and endocrinologists, when necessary, to optimise their readiness to conceive.



The procedure room at KKIVF@three, where eggs (oocytes) are retrieved from a woman's ovaries. This procedure is integral to assisted reproductive methods.

Coming Together To Tackle Metabolic Diseases In Women And Children

KKH gathers Asian key opinion leaders at the first Singapore Diabetes in Pregnancy Conference towards the expansion of research and collaboration for the management of metabolic diseases in women and children.



Guest-of-honour, Dr Amy Khor, Senior Minister of State for Health (left), receives a token of appreciation from Prof Tan Kok Hian, Chairman of the organising committee of the inaugural Singapore Diabetes in Pregnancy Conference.

In January 2018, KK Women's and Children's Hospital (KKH) organised the inaugural Singapore Diabetes in Pregnancy Conference, where key members from the KKH-led Integrated Platform for Research in Advancing Metabolic Health Outcomes in Women and Children (IPRAMHO), in partnership with the SingHealth Polyclinics and National Healthcare Group Polyclinics, met with members from the Maternal and Fetal Medicine Committee of the Asia and Oceania Federation of Obstetrics and Gynaecology to discuss extending the reach of IPRAMHO to countries in Asia and Oceania with high rates of gestational diabetes mellitus (GDM) and Type 2 diabetes. The new network aims to achieve a consensus of metabolic health screening approaches in countries in Asia and Oceania.

Senior Minister of State for Health, Dr Amy Khor, graced the two-day conference, which brought together over 200 clinicians, healthcare professionals and nurses and more than 20 key opinion leaders from Australia, China, Indonesia, Japan, Malaysia, Myanmar, Philippines, Singapore, Sri Lanka and Thailand.

"The conference was a great opportunity for discussion and the forging of collaborations on education and research into GDM, obesity and metabolic diseases among the regional leaders," shares Professor Tan Kok Hian, Head and Senior Consultant, Perinatal Audit and Epidemiology Unit, Department of Maternal Fetal Medicine, KKH, who is also the Chairman of the organising committee of the conference.

CLINICAL GUIDELINES LAUNCHED ON MANAGING GESTATIONAL DIABETES IN SINGAPORE

During the conference, the College of Obstetricians and Gynaecologists, Singapore also launched the nation's first clinical guidelines on managing GDM in pregnant women in Singapore – a metabolic disease with one of the highest incidence rates in Singapore.

The new guidelines recommend universal screening for GDM by 75gram Oral Glucose Tolerance Test between 24 to 28 weeks of a woman's gestation, and the adoption of the three-point International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria for diagnosing GDM.

KKH led in the development of the guidelines, which aim to guide obstetricians and gynaecologists in providing evidence-based care to pregnant women in Singapore.

Metabolic diseases such as obesity and diabetes are global issues in public health. Singapore has one of the highest incidences of GDM worldwide; based on current statistics, it is estimated that more than 6,000 pregnant women suffer from GDM each year, of whom more than 4,000 will develop diabetes in their lifetime.

In July 2017, KKH launched the IPRAMHO network to advance translational research in metabolic health in women and children, and spur collaboration between hospitals and primary healthcare providers to better prevent and manage metabolic diseases in Singapore. In September 2017, the Temasek Foundation Cares GDM Care programme was also introduced in KKH, which aims to pilot a novel model of care encouraging all pregnant women receiving antenatal care at the hospital to undergo GDM screening, and receive appropriate antenatal and postnatal care and follow-up to track and manage their diabetes condition.

"We are seeing encouraging results through KKH's initiatives; by working with our regional counterparts, we hope to discover new evidence-based, effective and affordable interventions that could provide early prevention and detection for metabolic diseases such as GDM in high-risk patient groups," says Prof Tan.

CELEBRATING 160 YEARS OF TRANSFORMING CARE for Women and Children



KK Women's and
Children's Hospital
SingHealth



1858-2018
Celebrating Our Heritage,
Shaping The Future

Since 1858, KK Women's and Children's Hospital has embarked on an ongoing journey to transform care and advance medical innovation, research and education, evolving from humble beginnings as a general hospital to become Singapore's leading tertiary referral centre for women and children today.

In 2018, as KKH commemorates 160 years of heritage in serving the community and caring for women's and children's health, we remain committed on our mission to deliver excellent, holistic and compassionate care for generations of women and children to come.

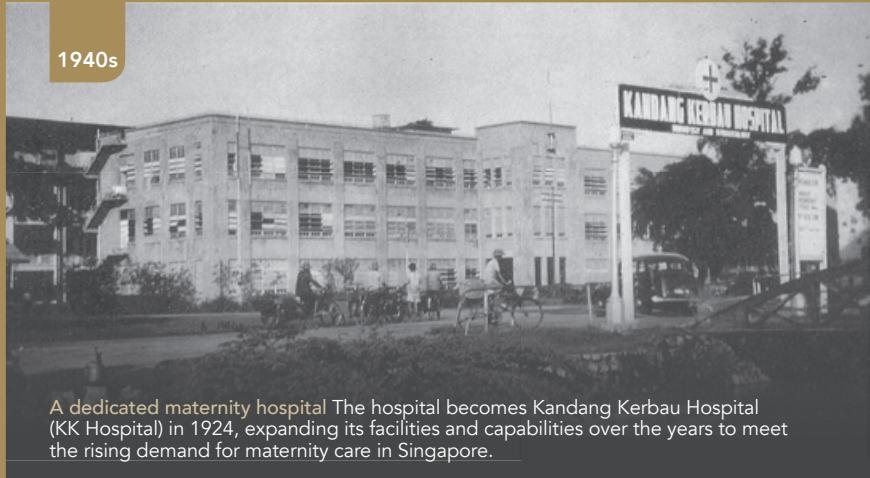
OUR FIRST 100 YEARS (1858 - 1957)

1858



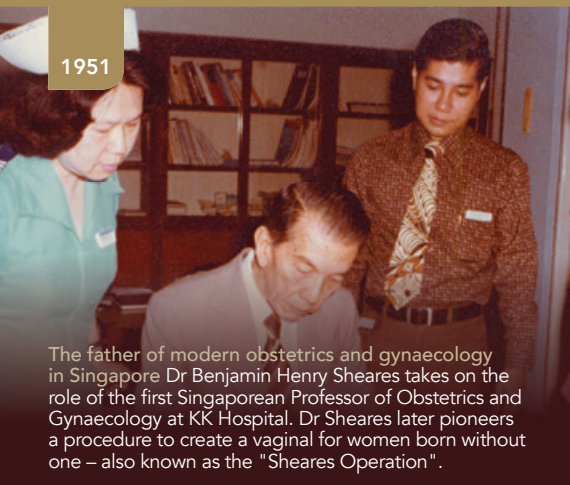
Our journey begins The modern-day KK Women's and Children's Hospital begins as the fifth general hospital in Singapore, built near the Kandang Kerbau area. Locals commonly referred to it as KK – Kandang Kerbau, which means "bullock pen" in Malay. In 1865, the hospital started seeing its first gynaecological and childbirth cases.

1940s



A dedicated maternity hospital The hospital becomes Kandang Kerbau Hospital (KK Hospital) in 1924, expanding its facilities and capabilities over the years to meet the rising demand for maternity care in Singapore.

1951



The father of modern obstetrics and gynaecology in Singapore Dr Benjamin Henry Sheares takes on the role of the first Singaporean Professor of Obstetrics and Gynaecology at KK Hospital. Dr Sheares later pioneers a procedure to create a vaginal for women born without one – also known as the "Sheares Operation".

1952



Training a new generation of local midwives KK Hospital launches Singapore's first School of Midwifery to equip midwives with essential skills to conduct labour and delivery for patients in the labour wards, as well as provide nursing care and health education to new mothers.

1955



Bringing care into the community During a nationwide baby boom, KK Hospital introduces Domiciliary Delivery and Aftercare Services to provide home-based antenatal care and help expectant mothers deliver safely at home.

ABOUT KK WOMEN'S AND CHILDREN'S HOSPITAL

KK Women's and Children's Hospital (KKH) is a recognised leader and Singapore's largest tertiary referral centre for Obstetrics, Gynaecology, Paediatrics and Neonatology. Founded in 1858, the 160-year-old academic medical institution leads in patient-centred management of high risk conditions in women and children. More than 500 specialists adopt a compassionate, multi-disciplinary and holistic approach to treatment, and harness medical innovations and technology to deliver the best medical care possible.

Accredited as an Academic Medical Centre, KKH is a major teaching hospital for all three medical schools in Singapore, Duke-NUS Medical School, Yong Loo Lin School of Medicine and Lee Kong Chian School of Medicine. The 830-bed hospital also runs the largest specialist training programme for Obstetrics and Gynaecology and Paediatrics in the country. Both programmes are accredited by the Accreditation Council for Graduate Medical Education International (ACGME-I), and are highly rated for the high quality of clinical teaching and the commitment to translational research.