Journal of General Practice
ISSN: 2329-9126

Abu-Amero et al., JGPR 2014, 2:3
DOI: 10.4172/2329-9126.1000158

Review Article Open Access

The Baby Bio Bank-A Legacy for Researchers Worldwide into Common Complications of Pregnancy

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Received date: Apr 04, 2014; **Accepted date:** Apr 14, 2014; **Published date:** Apr 20, 2014

Abstract

Two London Universities, University College London and Imperial College London, have established a biobank as a resource for investigating the four main complications of pregnancy (recurrent miscarriage, preterm birth, fetal growth restriction (FGR) and pre-eclampsia), that collectively affect about 20% of families trying to conceive. Samples are being taken from the three key members of the family, mother, father and baby, allowing hereditary factors from both parents to be tracked. Additional samples are being stored to allow parallel analysis of the functional mechanisms of pregnancy including the epigenetic, anatomical, physiological and even metabolic causes for the high loss of fecundity in man. http://www.ucl.ac.uk/babybiobank

Introduction

Collections of human biological samples from large cohorts of families with carefully collected phenotypic and clinical data allows detailed study of the mechanisms behind many diseases. For many years researchers have used animal models to understand the effects of genetic mutations on phenotype, but have often acknowledged that to translate knowledge fully to human disorders they must have access to corresponding matched human samples. There are some ethical barriers to overcome with humans but access to tissue samples post-surgery, a small extra blood sample during routine procedures and buccal/saliva swabs have provided invaluable material for human research. The Baby Bio Bank is focussing on the four main complications of pregnancy, recurrent miscarriage, preterm birth, FGR and pre-eclampsia.

The genetic and environmental mechanisms of growth and development in utero are complex as both genes and the environment have interacting effects. There have been many studies showing gene associations with complications of pregnancy, but due to small numbers of samples it is often difficult to draw definitive conclusions. The Baby Bio Bank (BBB) will provide the necessary number of samples for scientific research into complications of pregnancy in order to identify the genes and biological mechanisms involved. By creating a bioresource for national and international research, the BBB aims to provide samples of high quality so that data can be universally compared. It will also foster collaborative research to ensure the best use is made of the samples. By providing these samples as a biobank, the burden in terms of ethics applications, staff costs and recruitment for individual projects can be minimised.

Biobanking

Biobanking is defined as the collection and storage of samples and can vary from the collection of a single sample to millions, for individual use to global use and from simple generic to highly specialized collections. In most cases biobanks are established for the purpose of health research and translational medicine. This is the only sensible way forward for the study of complex, multifactorial diseases in humans where hundreds of samples are needed to elucidate function.

The UK hosts several large biobanks. The UK Biobank (http://www.ukbiobank.ac.uk) is perhaps best known, and its purpose is for specific research into diseases occurring in mid- to late life such as cancer, heart disease, diabetes, dementia, depression, osteoporosis, arthritis, Parkinson's disease and lung and kidney disorders. It has now recruited 500,000 individuals since its beginning in 2006, with 22 assessment centres around the country The UK Biobank collects and stores blood, urine and saliva with an extensive set of medical data on blood pressure, lung function and grip strength, height, weight and body mass, arterial stiffness, vision, hearing, family history of common diseases, bone density, diet and fitness.

Biobanks can also complement one another, such as the The Confederation of Cancer Biobanks (CCB-http://www.oncoreuk.org) which is a consortium of UK based organisations involved in the development, management and use of biobank resources for cancer research. The CCB also promotes the transfer of knowledge and experience amongst smaller biobanks to promote collaboration rather than competition. Other biobanks are more specialised, for example the Oxford Pregnancy Biobank, which collects maternal blood and urine, as well as clinical data such as scans, specifically for research

into micro- and nanoparticle biology in the search for new biomarkers in pre-eclampsia (http://www.obs-gyn.ox.ac.uk/research/ian-sargent).

The Baby Bio Bank

The BBB is directed by Professors Gudrun Moore (Institute of Child Health) and Lesley Regan (St Mary's Hospital, Paddington) supported by two clinical collaborators, Professors Catherine Williamson (Queen Charlotte's and Chelsea Hospital), Mark Johnson (Chelsea and Westminster Hospital), The BBB manager, Dr Sayeda Abu-Amero is responsible for all administrative aspects including HTA compliance, ethics application, annual reports, website management, biannual newsletter and management of the recruitment and sample management team. There are three recruiters (Ms Katherine Rogers, Drs Ana Maria Perez Miranda and Nita Solanky) working at the different hospital sites and they provide 24 hour cover to ensure as many samples are collected to complete trios as well as two sample management personnel (Drs Shawnelle White and Anna Thomas) responsible for sample barcoding, processing, quality control, storage as well as database entry.

The BBB has its own Research Management Board (RMB) currently chaired by Dame Joan Higgins which is responsible for ensuring all protocols are carried out according to national tissue bank ethics and the HTA and will also be responsible for determining which projects are successful at obtaining samples for future research.

Recurrent miscarriage is the loss of 3 or more consecutive pregnancies, and affects 1-2% of couples trying to have a successful pregnancy outcome [1]. While the actual number is difficult to quantify because of the nature of this complication, experts estimate there are at least 6,000 couples newly affected every year in the UK (according to the American College of Obstetrician and Gynaecologists) and miscarriages are the most common type of pregnancy loss (http://www.nhs.uk/conditions/miscarriage/Pages/Introduction.aspx).

One in every 13 babies is born before 37 weeks and is classed as a preterm birth. Prematurity is responsible for 80% of all neonatal deaths, and affects 30,000 babies in the UK annually. The rate of cerebral palsy in preterm babies is up to 30 times higher than in babies born at term. This incidence has not changed significantly in recent years, and prematurity represents a major health issue and challenge for modern obstetric care (http://www.nhs.uk/planners/pregnancycareplanner/pages/prematurelabour.aspx) [2].

Fetal Growth Restriction (FGR previously referred to as IUGR (intra-uterine growth restriction)) refers to a condition in which a fetus is unable to achieve its genetically determined potential size and affects 20,000 babies in the UK every year and this condition accounts for 50% of all stillbirths. Defining true fetal growth restriction (for example, by identifying falling intrauterine growth profiles) is difficult and defining a group of babies at or below the 10th percentile is often used as a proxy. Although 60% of these will turn out to be normal small babies, the remainder are at an increased risk of potentially preventable perinatal death. (http://www.patient.co.uk/doctor/Intrauterine-Growth-Retardation.htm) [3].

Pre-eclampsia is a multisystem disorder that typically presents with high blood pressure and proteinuria in the second half of pregnancy and is a leading cause of maternal death. Mild pre-eclampsia affects 4-6% of first time pregnancies with 1% of pregnant women experiencing severe pre-eclampsia [4]. Women who have pre-eclampsia in one pregnancy are at a higher risk of developing the condition in subsequent pregnancies. It is responsible for a considerable proportion of the 500,000 infant deaths per year worldwide and around six women in the UK die annually as a result of complications associated with pre-eclampsia (http://www.nhs.uk/Conditions/Pre-eclampsia/Pages/Introduction.aspx).

There is evidence that the four complications of pregnancy are part of a biological continuum which originates at the time of embryonic implantation with interrelated genetic and environmental factors influencing the final outcome of the pregnancy (Figure 1). Using samples collected by the BBB and advanced scientific technology capable of analysing many samples in parallel we can begin to dissect the biological, physiological, genetic and even epigenetic causes of these complications. The results should give rise to predictive biomarkers that might identify those most at risk prior to disease onset. This should offer the opportunity to design therapies to prevent disease or reduce the severity of adverse maternal and fetal outcomes associated with recurrent miscarriage, preterm birth, FGR and pre-eclampsia.

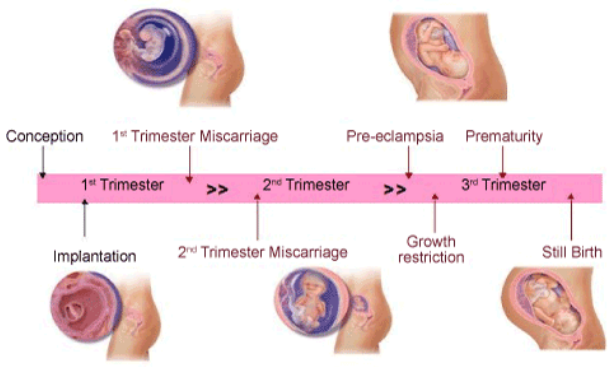

Figure 1: The four complications of pregnancy targeted by the BBB are a continuum.

The BBB collection will provide the biological materials for research into the causes of these and related pregnancy complications. The target of the BBB is to recruit 500 white European trios (mother, father and baby) from pregnancies affected by each complication plus 500 normal trios for comparative purposes giving a total of 2500 trios over the course of five years. Mothers and their partners are recruited in a variety of clinics but most often at their first booking in the antenatal clinic. Blood samples for DNA, serum and plasma, are collected from all consenting participants, plus urine from the mother. Where father is reluctant to give blood we the option of a saliva samples which provides high yields of excellent quality DNA [5]. The families are tracked throughout their pregnancy, and at the birth of the baby, we are notified and collect pieces of placenta, umbilical cord and cord blood. Where the baby is missed because delivery is at another hospital or any other reason, recruiters aim to get a buccal swab. Where no fetal sample is available-we are still able to use the maternal and/or paternal samples with available clinical information for other studies not looking at inherited genetic markers.

Ethical approval for the BBB was a straight forward process using the National Research Ethics Service (NRES) via the online Integrated Research Application System (IRAS-https://www.myresearchproject.org.uk/) and communications with Trent

Research Ethics Committee (REC) (new NRES committee name is East Midlands Derby 1 REC) have been efficient. We applied for Research Tissue Bank (RTB-https://www.myresearchproject.org.uk/help/ResearchTissueBanks.aspx) ethics which is voluntary and has the benefit that 'favourable ethical opinion applies to all research projects conducted in the UK using tissue or data supplied by the tissue bank, provided that the release of tissue or data complies with the attached conditions' (see https://www.myresearchproject.org.uk/help/Help%20Documents/PdfDocuments/researchtissuebank.pdf). This means that the BBB RMG are able to apply ethical approval to peer reviewed projects which relieves the potential research groups from the time consuming process of ethics application for their studies. Interested researchers are able to apply via the WoW BBB website (http://www.wellbeingofwomen.org.uk/research/baby-bio-bank/?menu=3c) where they submit a brief description of the proposal, type, number and amount of samples required, proof of funding and local R&D peer review. Applicants are also able to apply at the same time as applying for grants to help speed the research process. Applications are acknowledged by the BBB Manager and submitted to the BBB RMB for consideration every 4 months. Applicants are informed within 1 month of the BBB RMB meeting if their application is successful and samples dispatched within 3 months of approval. All applicants will have to submit an annual progress report and any unused samples must be returned to the BBB. The WoW BBB RMB recently met in March 2014 and approved the first three projects from within the UK-one with funding and two pending funding.

The hospitals in the BBB portfolio were selected as representing clinics with high proportions of pregnancies with complications. In addition, many research projects and clinical trials are also conducted in these (and other) hospitals for the ultimate benefit of the participant. The BBB recruiting staff put the wellbeing and satisfaction of the participant at the top of their list when considering recruitment as this is fundamental to the success of any biobank or research project involving patients [6].

BBB recruiters spending some time discussing the patient information sheet with the couple, giving the couple time to go home and discuss any issues if necessary before consenting and arranging for the bloods to be taken at the participant's convenience.

As all the samples are intended for DNA, RNA and protein isolation, they are being collected, processed and stored to the highest possible scientific standards. Quality control audits followed by downstream applications such as PCR, real-time PCR and sequencing has shown clearly that the samples are of high quality and can be used with confidence by researchers. The biological specimens have restricted value without the relevant clinical information for the pregnancy under investigation. We have ethical approval to include clinical information from the hospital databases relating to factors affecting pregnancy such as parental height, weight and relevant medical history such as diabetes, hypertension, and smoking. Importantly, we also collect fetal outcome data such as gestational age, birth weight, placental weight and mode of delivery. Consent is obtained from parents for access to their notes and information stored in the hospital database and also for any relevant queries which may be missing/unavailable to be followed up with the participants themselves. Currently, the BBB database stores detailed sample information (type of sample, amount or volumes available, date collected, time to process sample) in APOnline database, which is custom designed for the BBB (Assettrac-http://www.assettrac.co.uk/).

We have nearly reached our 2500 recruitment target (2448 mothers at the end of February 2014) with nearly 1,500 trios completed and available to researchers making it a unique resource as it stands today. We have >280 complete trios from recurrent miscarriage, preterm and pre-eclampsia and >200 from FGR. We will finish recruitment and collection by June 2014 and at that time will be able to publish a detailed breakdown of the BBB cohort. To date, only six participants from the 2500 who have participated have withdrawn indicating committed interest from the participants and public and satisfaction with BBB protocol, staff and information sheets.

The BBB is a unique collection of biological samples and medical data available for national and international researchers interested in understanding pregnancy complications. We opened on the 1st November 2013 and have approved the first three applications from interested researchers and have already received preliminary enquiries from a further ten. More information on the BBB is available at http://www.ucl.ac.uk/babybiobank including the BBB protocol and biannual newsletters. We welcome your applications.

Acknowledgement

The BBB would like to thank all participating hospital staff and families.

Contribution to Authorship

Sayeda Abu-Amero is the BBB Manager and wrote the manuscript. Anna Thomas and Shawnelle White are the BBB Sample Management team, Katherine Rogers, Ana Maria Perez Miranda and Nita Solanky are the BBB Recruiting Team. Lesley Regan and Gudrun Moore are the BBB Directors. Catherine Williamson and Mark Johnson are the BBB Clinical Investigators of the participating hospital sites. All other authors commented on the manuscript.

Details of Ethical Approval

The Baby Bio Bank has Tissue Bank approval (09/H0405/30) from Trent Research Advisory Committee (27th July 2009-2014).

Funding

The BBB is funded by the Wellbeing of Women (WoW-http://www.wellbeingofwomen.org.uk/research/baby-bio-bank/), a charity dedicated to improving the health of women and babies. The funds for the BBB were raised through the Lord Mayor's Appeal in 2007-2008 and has been supplemented with generous donations from the Mothercare Foundation. The funds raised cover the cost of six full time staff to recruit the 2500 trios and prepare the sample collection over five years, as well as the equipment for preparation and storage, and the processes to properly manage the bank.

References

1. Rai R, Regan L (2006) Recurrent miscarriage. Lancet 368: 601-611.
2. Plunkett J, Muglia LJ (2008) Genetic contributions to preterm birth: implications from epidemiological and genetic association studies. Ann Med 40: 167-195.
3. Al Qahtani N (2011) Doppler ultrasound in the assessment of suspected intra-uterine growth restriction. Ann Afr Med 10: 266-271.
4. Cantwell R, Clutton-Brock T, Cooper G, Dawson A, Drife J et al. (2011) Saving Mothers' Lives: reviewing maternal deaths to make motherhood

safer:2006-2008 The Eighth Report of the Confidential Enquiries into Maternal Deaths in the UK. BJOG 118 : 1-203.

5. Nunes AP, Oliveira IO, Santos BR, Millech C, Silva LP, et al. (2012) Quality of DNA extracted from saliva samples collected with the Oragene DNA self-collection kit. BMC Med Res Methodol 12: 65.

6. Gottweis H, Gaskell G, Starkbaum J (2011) Connecting the public with biobank research: reciprocity matters. Nat Rev Genet 12: 738-739.