Thalassaemia and other haemoglobinopathies are the causes of a major public health problem in many parts of the world. In Hong Kong, 4.3% of the pregnant population have α-thalassaemia trait while 2.8% have β-thalassaemia trait. If both couples are α-thalassaemia or β-thalassaemia minor, their foetuses will be at a 1 in 4 risk of developing homozygous α-thalassaemia or β-thalassaemia major respectively. The babies affected by homozygous α-thalassaemia often die towards the end of the pregnancy or soon after birth, and the pregnancies are often complicated by pre-eclampsia and postpartum haemorrhage. Individuals affected by β-thalassaemia have severe anaemia in infancy, require life long blood transfusion from around 9 months, suffer from problems of iron overload, and have a reduced life span of around 45 years. To prevent severe thalassaemias, prenatal screening for thalassaemia has been used worldwide.

We have shown that it is cost effective to run a universal prenatal screening programme in Hong Kong where both β-thalassaemia and α-thalassaemia are prevalent. In the study, 18,936 women were screened at our antenatal clinic and 153 couples were subsequently referred to our Prenatal Diagnostic Centre for counselling and further investigations. In addition, there were 238 tertiary referrals and 157 self referrals. After investigations, 84 foetuses were at risk of β-thalassaemia major/β-E thalassaemia, 19 of them were affected and 18 were aborted. The total expenditure on our programme (HK$ 10.0 million) would be less than the postnatal service costs (HK$ 40.4 million) for 18 β-thalassaemia major foetuses if they were born.

The algorithm in the prenatal screening of thalassaemia which has been adopted in the Prenatal Diagnostic and Counselling Department of Tsan Yuk Hospital is presented. After attending group counselling by clinic nurses, all women have blood sample taken for haemoglobin level (Hb) and mean corpuscular volume (MCV) as part of the antenatal routine blood investigations unless these investigations have already been performed. If maternal MCV is 80 fL or above, her foetus will be regarded as not being at risk of severe thalassaemia and no further assessment is needed. On the other hand, if maternal MCV is found to be low (<80 fL), the partner will be called for blood taking and arranged for an iron testing (including serum iron, percentage of transferrin saturation, and ferritin levels). The wife’s blood sample will be tested for Hb H inclusion bodies by incubation of red blood cells with brilliant cresyl blue. If the partner’s MCV is also low, the laboratory will determine the couple’s Hb A2 by micro-column chromatography and test the husband’s blood sample for Hb H inclusion bodies. β-thalassaemia trait is diagnosed by the finding of raised Hb A2 level (>3.5%). The presence of Hb H inclusion bodies is almost diagnostic of α-thalassaemia. If her partner’s MCV is normal (>80 fL), their foetus is regarded as not being at risk of severe thalassaemia and no further assessment is required. In the presence of a low MCV result and a normal iron status, a normal Hb pattern will not necessarily exclude α-thalassaemia and the woman or her partner will be managed as suspected α-thalassaemia trait. DNA analysis is required to confirm suspected cases.

If the couple has discordant thalassaemia traits, their foetus will not be at risk for serious thalassaemia unless one parent who carries β-thalassaemia trait has co-inheritance of α-thalassaemia. DNA analysis will be needed to exclude α-thalassaemia, the prevalence of which was reported as 7%. If the couple has β/ E thalassaemia traits, their foetus will be at 1 in 4 risk of having severe thalassaemia.

When iron deficiency is accompanied by a normal Hb A2 level and absent Hb H inclusion bodies, iron therapy will be given first, followed by repeat MCV four weeks later, before further investigations on their thalassaemia status are performed. There will be an increase in their Hb by 1 g/dl and an increase in MCV after iron therapy for four weeks. In the presence of iron deficiency, there is a possibility of missing concomitant thalassaemia trait because Hb A2 production may be depressed, and the brilliant cresyl blue preparation used for the detection of Hb H inclusion bodies may also be affected. However, Hb A2 level do not fall below the diagnostic range in Chinese women with concomitant β-thalassaemia and iron deficiency. Besides, iron deficiency is not present in any of the β-thalassaemia carriers and all of whom have elevated Hb A2 level. In addition, serial ultrasound examinations can be used to look for features of homozygous α-thalassaemia, thus saving the need and cost of DNA analysis to exclude the possibility of α-thalassaemia.

Routine Hb electrophoresis is not performed as part of the initial screening partly because of the cost and partly because there were no reported cases of sickle cell disease. Although some Hb E carriers whose MCV are above 80 fL
may be missed, there were also no reported cases of any β-thalassaemia syndrome born from a mother with MCV >=80fL in Hong Kong.

Several issues need to be considered for the implementation of the universal prenatal screening programme. First, doctors and nurses should be aware of the need for screening at risk ethnic groups. Many medical practitioners may not be aware of the screening procedures. Continuous medical education is needed. Second, the gestation at booking is important. Hospitals looking after predominantly pregnant populations with late or no antenatal care will need to shift antenatal to postnatal screening to ensure cost-effective screening for subsequent pregnancies. Third, different hospitals or obstetricians may not adopt the same cut off point of 80fl for MCV. It has been shown locally a MCV cut-off of <80fL detects all β-thalassaemia carriers and δβ-thalassaemia carriers in non-pregnant populations. Although a higher cut-off (85fL) for pregnant women has been suggested, there were no reported cases of Hb Bart’s disease born from a mother with MCV >=80fL. Fourth, uptake of prenatal diagnosis is affected by antenatal booking practice, region and ethnic group. A uniform policy across the territory on screening for haemoglobin disorders is needed.

References: