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Type 1 diabetes mellitus (T1DM) is the most common chronic metabolic condition in youth, and its incidence is increasing worldwide. Care of the child and adolescent with T1DM should be multidisciplinary and involve professionals experienced in childhood diabetes, including a physician, nurse, dietitian and social worker. Maintenance of excellent glycaemic control and regular screening for complications should be emphasized, all in the context of healthy and supportive physical and psychosocial environment.

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With the advent of routine prenatal ultrasound, the detection of ovarian mass has become common. Large ovarian cysts that are 5 cm or more are estimated to occur in 0.5-2 per 1000 pregnancies. Torsion of the ovary is the total or partial rotation of the adnexa around its vascular axis or pedicle.

Sreelatha Sampath Kumar, Vedavathy Nayak, Prathiba, Ashwini Rani

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Prematurity is defined as birth before 37 completed weeks of gestation (259 days). The condition is the leading cause of neonatal mortality and morbidity. Very preterm birth is birth <32 weeks and extremely preterm birth occurs before 28 weeks of gestation. Preterm birth remains one of the most intractable problems that contribute to perinatal morbidity and mortality throughout the world.

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304 Current Management of Antenatal Hydronephrosis- An Update
Antenatal hydronephrosis (ANH) is the most commonly diagnosed congenital urinary tract anomaly, which is detected by prenatal screening in 1–5% of all pregnancies. In the early years of routine fetal ultrasound screening, almost all cases of ANH were subjected to invasive imaging studies postnatally, followed by a pre-emptive surgical approach. The management of ANH has trended towards a more conservative approach over the past two decades.
Yap Te-Lu, Anette Sundfor Jacobsen

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Hydatidiform mole, hCG concentrations, and chemotherapy

In the UK, hydatidiform moles constitute between 1 and 3 of every 1,000 pregnancies, but they are more common in east Asia. They are more common in younger (<16 years) and older (>45 years) women. Molar pregnancies present with vaginal bleeding in the first trimester, and levels of human chorionic gonadotropin (hCG) in serum and urine are raised. Following dilatation and curettage, hCG levels return to normal in about 92% of cases. Malignant transformation occurs in about 15% of cases after complete hydatidiform mole and 0.5–1% after partial hydatidiform mole. Chemotherapy, usually with methotrexate or dactinomycin, is then necessary. All women with a hydatidiform mole in the UK are referred for hCG monitoring and surveillance to one of three national centres in Dundee, Sheffield, and London. Post-mole gestational trophoblastic neoplasia is suspected when hCG levels plateau or increase or remain raised at 6 months although they are falling. Evidence suggests, however, that an increased but falling hCG level at 6 months after uterine evacuation may not necessarily necessitate chemotherapy. A retrospective study at a single hospital in London, England, has added support to this suggestion.

The study included 13,960 women with a diagnosis of hydatidiform mole between January 1993 and May 2008. Among these women, 76 (<1%) had persistently high (>5 IU/L) hCG levels at 6 months. Sixty-six of these patients continued under surveillance, and hCG levels returned to normal without chemotherapy in 65 (98%). The one patient whose hCG levels remained high had chronic renal failure as a cause of the high levels and remained otherwise well. Ten patients received chemotherapy, and hCG levels returned to normal in eight of them (80%). The remaining two patients had persistent, slightly high (6–11 IU/L) levels, but there were no associated clinical problems off treatment. There were no deaths, and outcomes were similar with or without chemotherapy.

These researchers conclude that a policy of continued surveillance without chemotherapy seems acceptable for patients with raised (not very high) but falling hCG levels at 6 months after evacuation of a hydatidiform mole.

Effectiveness of trained traditional birth attendants

Traditional birth attendants are in charge at many births in developing countries, and giving them extra training and resources can improve obstetric and neonatal outcomes. A meta-analysis of six randomized controlled trials and seven non-randomized studies has confirmed that training these workers results in improved results.

A total of 138,549 patients were included in the randomized trials that assessed the effects of training and support for traditional birth attendants. Meta-analysis showed significant reductions of 24% in perinatal mortality and 21% in neonatal mortality after such training and support. The non-randomized trials included 72,225 patients. Meta-analysis showed significant reductions of 30% in perinatal mortality and 39% in neonatal mortality. Meta-analysis of six studies of maternal mortality showed a non-significant reduction of 20% after training and support of traditional birth attendants.

Training and support of traditional birth attendants in developing countries improves outcomes according to the type and extent of training and support provided. Perinatal, neonatal, and maternal mortalities may all be improved.

Home vs hospital birth in England

A national prospective cohort study in England has confirmed the safety of planned home birth for low-risk women.
The study included 64,538 women with low-risk pregnancies with delivery between April 2008 and April 2010. The primary outcome was a composite of perinatal death, and intrapartum morbidity (stillbirth during labour, early neonatal death, neonatal encephalopathy, meconium aspiration syndrome, brachial plexus injury, or fractures of humerus or clavicle). Overall, the incidence of the primary outcome was similar for births planned at home (4.2 primary outcome events per 1,000 births), in an obstetric unit (4.4 per 1,000), and in a midwifery unit (3.5 per 1,000). On subgroup analysis, planned place of birth had no significant effect on outcomes among multiparous women. Among nulliparous women, the incidence of primary outcome events was greater for planned home deliveries (9.3 per 1,000) than for deliveries planned on an obstetric unit (5.3 per 1,000) or on a midwifery unit (4.5 per 1,000). Transfers from home or midwifery unit to an obstetric unit were necessary more often for nulliparous women. Operative and instrumental deliveries were more frequent for deliveries planned to be in an obstetric unit.

For low-risk pregnancies in multiparous women, home birth or birth in an obstetric unit is generally safe and there is a lower risk of obstetric intervention. Among nulliparous women, there is a higher risk of poor outcomes with home birth.


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**PAEDIATRICS**

Extended nevirapine for breastfeeding infants of HIV-infected mothers

Although breastfeeding is essential in sub-Saharan Africa for the infant’s nutrition and protection from infection, prolonged breastfeeding may lead to mother-to-child transmission of human immunodeficiency virus (HIV) 1. Antiretroviral therapy is given to protect against antenatal and intrapartum HIV transmission, but prolonged prophylaxis during breastfeeding has been difficult to achieve in many countries. Now, successful prophylaxis during breastfeeding has been reported from South Africa, Tanzania, Uganda, and Zimbabwe.

The study included 1,527 breastfeeding infants of HIV-1-positive mothers. The infants received oral nevirapine suspension for the first 6 weeks. Those who were HIV-negative at 6 weeks were then randomized to continued nevirapine, or placebo, until the age of 6 months or until stopping breastfeeding. Between the ages of 6 weeks and 6 months, HIV-1 infection was acquired by 1.1% in the extended nevirapine group and 2.4% in the placebo group, a significant 54% improvement with extended nevirapine. At 6 months of age, mortality, combined mortality and HIV-1 infection, and severe adverse event rates were similar in the two groups.

Extended nevirapine prophylaxis given to the breastfeeding infant is effective for at least 6 months. It should be used along with other provisions such as routine HIV screening in pregnancy, and antiretroviral interventions during pregnancy, labour, and delivery.

INTRODUCTION

Type 1 diabetes mellitus (T1DM) is the most common chronic metabolic condition in children and adolescents. Diabetes mellitus (DM) comprises a group of heterogeneous conditions involving defects in insulin secretion or action, or both, resulting in hyperglycaemia and associated abnormalities in carbohydrate, protein and fat metabolism. The classification of DM is described by the American Diabetes Association. T1DM is by far the most common type seen in childhood. The incidence of type 2 diabetes (T2DM) is increasing most notably in the adolescent age group, in parallel with the rise in obesity throughout the world.

EPIDEMIOLOGY

Worldwide, there are approximately 480,000 children with T1DM, and 76,000 new cases are diagnosed each year. Incidence rates of T1DM in children and adolescents under 15 years of age vary greatly by geographical region, from the highest in Finland (57.4/100,000/year) and Canada (21.7/100,000/year) to the lowest reported in China (0.6/100,000/year) and Venezuela (0.1/100,000/year). The overall annual incidence is increasing at a rate of about 3% with the greatest increase in the youngest age group. Several hypotheses to explain this changing incidence have been proposed, such as rapid growth in early childhood, environmental exposures, and reduced early exposure to pathogens, but none is widely accepted. Data are lacking about the incidence of T1DM in some developing countries in sub-Saharan Africa and South and East Asia, in which the diagnosis may be being missed. T1DM affects children of all ages, both sexes, and all ethnic groups.
T1DM is the result of a combination of genetic and environmental influences. It most commonly results from autoimmune destruction of insulin-producing β-cells in the pancreas. Devendra et al proposed that one or more environmental factors, such as enteroviruses, dietary factors or toxins, might trigger the development of T-cell-dependent autoimmunity in genetically susceptible individuals. Autoimmunity is manifest by detectable antibodies to ICA512/IA-2, insulin autoantibody and glutamic acid decarboxylase. Insulitis with gradual β-cell destruction leads to pre-diabetes and finally to overt DM. These patients are susceptible to other autoimmune diseases, such as Hashimoto’s thyroiditis, coeliac disease, Addison’s disease, and myasthenia gravis.

Forty genetic loci have been associated with T1DM by a genome-wide association study and meta-analysis. A number of genetic loci in the major histocompatibility region are associated with increased susceptibility to developing T1DM, including the alleles DR3/4, DQ 0201/0302, DR 4/4, and DQ 0300/0302. The risk of T1DM is approximately 5% if there is an affected first-degree relative and slightly higher if the affected parent is the father rather than the mother. To date, interventional trials have failed to delay the onset or prevent T1DM in those genetically at risk. Ongoing research by international networks is exploring ways to prevent, delay or reverse the progression of T1DM (eg, TrialNet, TRIGR).

**CLINICAL PRESENTATION AND DIAGNOSIS**

The presentation of T1DM can range from a clinically stable child with symptoms of polyuria, polydipsia, enuresis and weight loss to a severely dehydrated child with diabetic ketoacidosis (DKA). In the presence of these classical symptoms of hyperglycaemia, a single blood glucose measurement > 11.1 mmol/L is sufficient to make the diagnosis of DM. In such situations, the diagnosis should not be delayed; treatment should be initiated urgently to prevent or reverse DKA. Only rarely are repeated blood glucose measurements and/or an oral glucose tolerance test required to make the diagnosis of T1DM in children (Table 1).

**Type 2 Diabetes (T2DM)**

In the pubertal age group, T1DM must be differentiated from T2DM. A Canadian population-based surveillance study of non-type 1 diabetes in children under 18 years of age found an incidence rate of 1.55/100,000/year. The aetiology of T2DM is multifactorial, but key factors include genetic predisposition (> 80% have a positive family history), ethnicity (more common in African-American, Asian, Hispanic and Native North Americans), obesity, intrauterine environment, sex, and insulin resistance. Both secretion and action of insulin are usually dis-
Figure 1. Emergency room (ER) management guidelines for the child with type 1 diabetes in diabetic ketoacidosis (DKA)

**History** (some or all of)
- Polyuria
- Polydipsia
- Weight loss
- Abdominal pain
- Tiredness
- Vomiting
- Confusion
- Difficulty breathing
- Urine ketones/glucose
- Capillary glucose STAT in ER
- Venous blood – glucose, gases, electrolytes, urea, creatinine
- Other as indicated

**Confirm DKA**
- Ketonuria
- Serum bicarbonate <18 mmol/L
- Glucose >11 mmol/L
- pH <7.3
- Consult paediatrician immediately

**Vascular decompensation** (with or without coma)
- Minimally dehydrated
- Tolerating fluids orally
- Normal bowel sounds
- Normal mental status

**Normal saline**
- 7 mL/kg over 1st hour with potassium chloride as noted below THEN 3.5–5 mL/kg/hr

**Resuscitation**
- Assess airway and breathing
- Apply 100% oxygen by mask
- Normal saline 10 mL/kg to expand vascular space
- Decrease to 5–7 mL/kg/hr with potassium chloride as noted below
- Only infuse sodium bicarbonate (1–2 mEq/kg over 1 hour)
- Life-threatening hyperkalaemia
- Inotropic-resistant shock
- Cardiac arrest

**Acidosis not improving** (in 3–4 hours)
- Check insulin delivery system
- Consider sepsis
- Contact Tertiary Pediatric Diabetes Centre
- Treat for cerebral oedema
- 20% mannitol 5 mL/kg over 20 minutes
- If sodium has declined, administer 2–4 mL/kg of 3% saline over 10–20 min
- Normal saline at maintenance IV rate
- Decrease insulin to 0.04–0.05 U/kg/hr = 0.4–0.5 mL/kg/hr of standard solution as above
- Contact Tertiary Pediatric Diabetes Centre
- Admit to ICU

**Acidosis improving**
- Blood glucose <15 mmol/L
- OR
- Blood glucose falls >5 mmol/l/hr after 1st hour of fluids:
  - Change IV to D5
  - Increase insulin to 0.04–0.05 U/kg/hr = 0.4–0.5 mL/kg/hr of standard solution as above
  - Blood glucose = 10 mmol/l/hr
  - Change to IV fluids

**Neurological deterioration**
- Headache, irritability, decreased level of consciousness, decreased HR
- First rapidly exclude hypoglycaemia by capillary blood glucose measurement
- Treat for cerebral oedema

**Observation and monitoring**
- Hourly blood glucose (capillary)
- Aim for a decrease in blood glucose of 5 mmol/L/hr
- Strict hourly documentation of fluids input/output
- Calculate and review fluids balance at least every 4 hours

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  - Blood glucose = 10 mmol/l/hr
  - Change to IV fluids

- Start S/C insulin
- Stop IV insulin ½ hour after S/C dose of rapid-acting or 1 hour after S/C dose of regular insulin
- Determine cause of DKA
- Admit to ICU

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- Consider sepsis
- Contact Tertiary Pediatric Diabetes Centre
- Treat for cerebral oedema
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- Aim for a decrease in blood glucose of 5 mmol/L/hr
- Strict hourly documentation of fluids input/output
- Calculate and review fluids balance at least every 4 hours


BP = blood pressure; D5 = 5% dextrose; EKG = electrocardiography; HR = heart rate; ICU = intensive care unit; IV = intravenous; PALS = Pediatric Advanced Life Support; Q2–4h = every 2–4 hours; S/C = subcutaneous; STAT = statim.
ordered at clinical presentation, although one feature may predominate. Insulin resistance may manifest clinically with acanthosis nigricans (a velvety thickening of the dermis found especially on the posterior neck and axillae), features of polycystic ovarian syndrome (hyperandrogenism, menstrual irregularity), and features of metabolic syndrome (hypertension, dyslipidaemia, and obesity).

**Monogenic Diabetes**

Occasionally, T1DM must be differentiated from monogenic diabetes, formerly known as maturity-onset diabetes of the young. Monogenic forms of diabetes result from single gene mutations that cause impaired β-cell function or, rarely, severe insulin resistance. Identifying this diagnosis is important to predict the course of disease, explain associated clinical features, guide management, and aid in diagnosis and management of similarly affected family members. Monogenic diabetes should be considered in the following clinical scenarios:

- Neonatal diabetes and diabetes diagnosed within the first 6 months of life
- Familial diabetes with an affected parent
- Mild (5.5–8.5 mmol/L) fasting hyperglycaemia, especially if young or familial
- Diabetes associated with extra-pancreatic features
- Specific genetic defects are listed in Table 1, and genetic testing is available for all of the identified mutations.

**DIABETIC KETOACIDOSIS**

Diabetic ketoacidosis results from absolute insulin insufficiency, leading to metabolic acidosis (pH < 7.3 or bicarbonate < 15 mmol/L), hyperglycaemia (blood glucose > 11 mmol/L), ketonaemia, and ketonuria. DKA is present at T1DM presentation in 15–67% of children, its frequency being inversely related to the incidence of T1DM in that area. In those with established T1DM in the United States, the incidence of DKA has been reported to be 8 episodes per 100 patient-years. Risk factors that predict DKA include female sex, longer duration of diabetes, higher mean HbA₁c, higher reported insulin dose, the presence of psychiatric disorders, insulin omission or insulin pump failure. DKA may also be present in up to 25% of young people presenting with T2DM.
DKA should be treated as a medical emergency by an experienced medical team. The treatment algorithm used at our centre is outlined in Figure 1. Treatment of DKA in children differs in several respects from that in adults: first, both fluids and insulin are calculated on a per kilogram rather than an empirical basis. Fluid repletion should occur gradually with sodium chloride 0.9%. Boluses of fluid and insulin should be avoided. Bicarbonate should be given only in the setting of life-threatening hyperkalaemia, inotrope-resistant shock, or cardiac arrest.

DKA is the major cause of hospitalization, morbidity and mortality in young people with T1DM. The most serious complication is cerebral oedema, which occurs in 0.5–1.0% of DKA episodes, with 25% mortality. Demographic risk factors associated with increased risk for cerebral oedema include younger age, new-onset diabetes, and longer duration of symptoms. Risk factors that are present at the time of diagnosis or during treatment are increased serum urea, severe acidosis, greater hypocapnia after adjusting for the degree of acidosis, administration of sodium bicarbonate, and an attenuated rise in the measured serum sodium during treatment.

**MANAGEMENT OF T1DM IN CHILDHOOD**

The diagnosis of T1DM is a pivotal moment for the child as well as for his/her family. T1DM is a lifelong condition with serious short- and long-term implications. It is essential that from the moment of diagnosis, these families receive expert care from a team of health professionals experienced in childhood diabetes, including a physician, diabetes nurse, dietitian and social worker.

At onset, children presenting without DKA can be safely managed on an ambulatory basis provided that support services are available and that no other medical or social conditions exist that would place the child in danger. A meta-analysis of home-based management at DM onset suggests that in comparison to routine hospital admission, outpatient care is not associated with worse metabolic control, acute diabetic complications or psychosocial outcomes, or greater costs. Early ‘survival skills’ to be mastered include insulin injections, blood glucose monitoring, basic nutrition planning, and detection and treatment of hypoglycaemia. In the subsequent weeks, more detailed information is provided about diabetes management (pathophysiology, insulin dose adjustment, effects of exercise, and sick days).

Insulin initiation varies greatly among different centres but generally consists of two to four injections per day. The starting total daily dose is 0.4–0.6 units/kg body weight/day, usually lower in younger children, and is adjusted on a daily basis until target blood glucose is achieved (Table 2). Families of children with T1DM should have a clear understanding of the rationale for blood glucose and HbA1c targets for their child.

After initial stabilization and education, children and their families enter the long-term follow-up phase of their diabetes. This includes regular
follow-up visits with their diabetes team with surveillance for psychosocial problems, associated conditions (hypothyroidism, coeliac disease), and microvascular and macrovascular complications. Special attention must be paid to those children and their families, most frequently the youngest children and adolescents, who have the greatest difficulty meeting the considerable demands of their diabetes regimen.

Soon after initial presentation, most patients enter a transient remission or ‘honeymoon’ phase when exogenous insulin requirements decrease as a result of residual β-cell secretion. The duration of the honeymoon phase is proportional to the age of the child. Families need to be forewarned of the natural history of T1DM so that they do not develop false hope that their child’s diabetes is ‘going away’.

GLYCAEMIC AND HbA1C TARGETS

The Diabetes Control and Complications Trial (DCCT) demonstrated conclusively that intensive glycaemic control delays and prevents the microvascular and macrovascular complications of T1DM.\(^{16,17}\) Intensification of therapy is associated with an increased risk of hypoglycaemia that can be a limiting factor in achieving good metabolic control. Severe hypoglycaemia in young children has been associated with mild cognitive deficits later in life, although the cause-and-effect relationship remains controversial. This demands that age-appropriate targets be set and that progressively tighter control be sought as the child grows older. Table 2 summarizes the glycaemic goals published in the 2008 Clinical Practice Guidelines of the Canadian Diabetes Association.\(^{18}\) Multiple studies attest to the difficulties in achieving these goals in all children with T1DM.\(^{19,20}\)

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid-acting</td>
<td>10–30 min</td>
<td>30 min–3 h</td>
<td>3–5 h</td>
</tr>
<tr>
<td>Lispro</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspart</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short-acting</td>
<td>30–60 min</td>
<td>2–5 h</td>
<td>Up to 12 h</td>
</tr>
<tr>
<td>Regular human insulin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate-acting (NPH)</td>
<td>90 min–4 h</td>
<td>4–12 h</td>
<td>Up to 24 h</td>
</tr>
<tr>
<td>NPH human insulin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal insulin</td>
<td>45 min– Minimal</td>
<td>Up to 24 h</td>
<td></td>
</tr>
<tr>
<td>Glargine</td>
<td>4 h</td>
<td>peak action</td>
<td></td>
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<tr>
<td>Detemir</td>
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</table>


INSULIN REGIMENS

Approaches to insulin therapeutics vary from one centre to another. Most children and teenagers now start their treatment with a combination of intermediate-acting insulin or basal insulin analogue (insulin glargine or insulin detemir), combined with rapid-acting insulin analogues (insulin lispro or insulin aspart) given two or more times daily, with insulin doses calculated to match carbohydrate intake and ambient blood sugar. The choice of regimen should be tailored to the child’s age, duration of diabetes, daily routines, targets of metabolic control, and individual and family preferences.\(^{21}\) When rigorously applied, this basal-bolus approach can help to achieve and maintain near-normal glycaemia. See Table 3 for the onset, peak, and duration of action of commonly used insulin preparations.

Increasingly, children and teenagers with T1DM are using continuous subcutaneous insulin infusion (CSII) pumps.\(^{22}\) CSII is a more sophisticated form of basal-bolus regimen whereby fast-acting insulin analogue is administered by continuous in-
fusion (basal rate) with intermittent boluses given before carbohydrate ingestion or to correct hyperglycaemia. A systematic review and meta-analysis of randomized controlled trials comparing CSII to multiple daily injection in children with T1DM found a modest improvement (0.24%) in HbA1c in the CSII group and found no differences in DKA or severe hypoglycaemia between groups.5 Quality of life and patient satisfaction have been reported to be at least equal or improved with CSII.6 The cost of CSII is considerable and cannot be accommodated by many families and health-care systems.

BLOOD GLUCOSE MONITORING

Children and adolescents with T1DM are encouraged to monitor blood glucose at least four times per day (before each meal and at bedtime). Maintenance of a blood glucose logbook is essential to follow patterns and to make appropriate dose adjustments. Continuous glucose monitoring technologies have been developed and are increasingly being used in clinical care as an adjunct to intermittent monitoring.23

HbA1c is a measure of glycaemic control over the previous 4–12 weeks, weighted more heavily toward the most recent 4 weeks. Lower HbA1c values have been associated with fewer and delayed microvascular and macrovascular complications.16,17 The goal of diabetes management should be to maintain the lowest possible HbA1c without severe or prolonged hypoglycaemia or hyperglycaemia.

NUTRITION

Recommendations for nutritional intake in young people with T1DM should aim to support optimal glycaemic control, blood pressure, and lipid profiles, and fit with the insulin regimen.24 If carbohydrate counting is used, insulin doses can be calculated based on the number of grams of carbohydrates consumed and on deviation from the target blood glucose. Nutritional requirements for children with T1DM do not differ from those of healthy children and adolescents.25

PHYSICAL ACTIVITY

Physical activity in general leads to increased glucose utilization, although in some cases rigorous exercise may induce a stress response leading to hyperglycaemia. For children and teenagers involved in exercise activities, more frequent monitoring with either insulin dose adjustment or appropriate food intake are needed to avoid the extreme hypoglycaemia that can occur with activity. Diabetes should not limit the ability of a child to participate in sport. Methods for adjusting insulin and carbohydrate intake to accommodate exercise have been proposed.26,27

HYPOGLYCAEMIA

Hypoglycaemia (blood glucose < 3.9 mmol/L or 70 mg/dL) is a common unwanted effect in people treated with insulin and occurs when there is an imbalance in insulin dose, food consumed and activity. Symptoms include autonomic (adrenergic) activation and/or neurological dysfunction (neuropglycopenia).28 Recognition of symptoms of hypoglycaemia can be difficult in young children with T1DM, and therefore increased monitoring of blood glucose when hypoglycaemia might be expected (overnight, after insulin dose adjustment, strenuous exercise, or illness) is recommended. Families should have injectable glucagon at home to treat severe hypoglycaemia (coma, seizure, or severe confusion). Hypoglycaemia has been associated with reduced cognitive functioning and can, rarely, be a cause of death in young people with T1DM. Co-morbidities...
such as coeliac disease and Addison’s disease can increase the risk of hypoglycaemia.

**SICK-DAY MANAGEMENT**

Diabetes control may deteriorate during periods of intercurrent illness. Illnesses associated with decreased oral intake may predispose to hypoglycaemia. Alternatively, the stress of some illnesses may lead to a vigorous counter-regulatory hormone response, leading to hyperglycaemia and ketosis. Frequent monitoring of blood glucose and ketones, continuation of insulin therapy with appropriate dose adjustment, and timely emergency department attendance for those with repeated vomiting should help to prevent metabolic deterioration.

**ADOLESCENTS WITH T1DM**

Given the association of smoking with both microvascular and macrovascular complications of DM, adolescents should be counselled in smoking prevention and cessation. It is important to address the risk of severe hypoglycaemia associated with an unpredictable daily activity schedule, intensification of the insulin regimen, and the effect of alcohol and illicit drugs on blood glucose. Adolescents who plan to or hold a driver’s licence should always check their blood glucose before driving. Unstable glycaemic control and severe hypoglycaemic events may limit their ability legally to obtain or maintain a driver’s licence.

Adolescents should be offered regular sexual health and contraception counselling. Poorly controlled T1DM is a risk factor for maternal and fetal complications. Diabetes is not an absolute contraindication to using oral contraception. Depression, body image concerns, and higher body mass index percentile in teenage girls with T1DM have been shown to predict the onset of eating disturbances and disorders and should therefore be assessed in the routine diabetes care in this population. Insulin omission may be one method by which the teenager may attempt to control his/her weight.

**TRANSITION TO ADULT CARE**

The transition period from paediatric to adult DM care can be a daunting time for the patient and family. In anticipation of this, adolescents with DM should be encouraged to take an increasingly active role in their diabetes care from an early stage. Teenagers should also have private time with the members of the diabetes care team as this promotes independence and responsibility. In the context of universal health-care funding, there is an increased rate of DM-related hospitalizations in the 2 years after transition to adult care, although the risk is less for youth who transfer to a new allied health team but maintain physician continuity. Formal transition programmes may facilitate transfer to adult care and prevent the high rates of drop-out reported in some centres.

**COMPLICATION SURVEILLANCE**

Chronic hyperglycaemia is associated with subsequent development of microvascular complications (retinopathy, neuropathy and nephropathy). Tight metabolic control delays and slows the progression of these complications. Suboptimal metabolic control has been shown to have an enduring negative effect on the development and progression of microvascular complications even if glycaemic control is subsequently ameliorated, a phenomenon termed metabolic memory. Other risk factors for long-term complications include younger age of DM onset, longer duration of disease, smoking, hypertension, dyslipidaemia, and family history.

DM is also a major risk factor for macrovas-
cular complications (coronary artery, peripheral artery, and cerebrovascular disease). Cardiovascular disease is the most important cause of the excess mortality associated with diabetes. Preventive measures include maintaining normal blood pressure, correcting dyslipidaemia, avoiding smoking, and participating in regular exercise.

Recommendations for screening for complications are summarized by the Canadian Diabetes Association 2008 Clinical Practice Guidelines. Trials are ongoing to determine whether, in addition to optimizing glycaemic control, pharmacological interventions for high-risk young people with T1DM will provide cardio-renal protection. Patient and family education about complications should begin early and be ongoing, emphasizing the proven benefit of excellent glycaemic control.

**FUTURE DEVELOPMENTS**

Pancreatic and islet-cell transplantation has been performed in adults with T1DM for end-stage renal disease or persistent metabolic instability. These procedures carry significant risks related to the procedures themselves and the need for chronic immunosuppression. Furthermore, only 10% of patients were insulin-independent at 5 years after islet-cell transplantation.

Research to develop an effective extracorporeal artificial pancreas is ongoing. This system involves an insulin pump to deliver insulin, a continuous glucose sensor, and an effective algorithm to alter insulin delivery based on real-time glucose sensor inputs.

Other strategies to improve the effectiveness of subcutaneous insulin action in T1DM have been proposed, including insulin-sensitizing therapies such as recombinant human insulin-like growth factor 1, growth hormone suppressors or antagonists, and direct insulin-sensitizing agents (metformin, thiazolidinediones). Other agents that may improve postprandial blood glucose, such as amylin analogues (pramlintide), alpha glucosidase inhibitors (acarbose), and glucagon-like peptide 1 analogues have also been studied. The long-term safety and effectiveness of these agents for the management of T1DM in young people remain uncertain.

**CONCLUSION**

T1DM in young people remains a common and challenging condition. Advances continue in the understanding of the pathogenesis of DM, especially in the area of genetic susceptibility. Significant improvements have been made in the development of glucose monitors, insulin formulations and delivery systems, and the organization of health services. These substantial advances should be made known to young people and their families as reason for hope, and as an impetus to maintain the best possible metabolic control. A multidisciplinary approach to the care of young people with T1DM should

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**What’s new?**

- The incidence of type 1 diabetes mellitus (T1DM) is increasing worldwide at a rate of approximately 3% per year with the greatest increase in the youngest age group
- Genetic loci associated with T1DM are being discovered by genome-wide association studies
- In the management of diabetic ketoacidosis, bicarbonate should be given only in the setting of life-threatening hyperkalaemia, inotrope-resistant shock, or cardiac arrest
- Despite advances in monitoring devices, insulin preparations and delivery mechanisms, many children and adolescents (especially with T1DM fail to achieve their age-appropriate glycaemic targets
- Ongoing research in the area of islet-cell transplantation, closed-loop insulin delivery systems, and insulin-sensitizing and other adjunctive agents may lead to improved therapies for the management of T1DM in the future
emphasize optimal metabolic control with minimal hypoglycaemia, in the context of a healthy and supportive physical and psychosocial environment.

FURTHER READING


REFERENCES


About the Authors

Rayzel M Shulman is currently pursuing a PhD at the University of Toronto, Ontario, Canada. Competing interests: Rayzel Shulman received the 2009/10 Canadian Pediatric Endocrine Group (CPEG) Fellowship sponsored by Novo Nordisk Canada. Denis Daneman is Paediatric-in-Chief at SickKids and Chair of the Department of Pediatrics at the University of Toronto, Ontario, Canada. Competing interests: Denis Daneman has been a member of the Hvidøre International Study Group for Childhood Diabetes sponsored by Novo Nordisk Inc.
A 24 years old, second gravida, Muslim woman presented in labour ward with generalized swelling and giddiness and breathlessness at 36 weeks and 02 days of gestation. She was a booked case from first trimester, had three ANC visits. 5 years ago she delivered a live full term male baby normally vaginally without any complication. She belonged to a poor socio economic strata. She had no history of use of drugs which can cause pancytopenia. Her diet during this time had consisted with wheat roti and rice, with no folate-containing foods. She has defaulted her follow up and ANC advices.

Her examination at admission showed anasarca and raised BP to 150/96 mm of mercury with urine albumin of 3+. Her uterine size revealed lag of 02 weeks from period of gestation. Her admission test (NST) was reactive, USG showed IUGR of 02 weeks with oligohydromnios (Amniotic Fluid Index- 02 ), though her color doppler study was normal. Her fundoscopy examination was also normal.

Full blood haemogram at admission showed a severe macrocytic anaemia , thrombocytopenia and leucopenia. Haemoglobin 5.6g/dl, mean cell volume 82.2fl, mean cell haemoglobin 25.7pg, MCHC 30.9gm/dl, TLC 2400/cumm, platelets 22000/cumm. Her prothrombin time was deranged (Blood did not clot even for 24 Hours) Blood film showed anisocytosis and polychromasia with megaloblastic and dysplastic erythroblasts, hypersegmented neutrophils, some myelocytes and promyelocytes and an occasional blast and the picture of pancytopenia however there was no parasite seen. The film confirmed the markedly reduced platelet count. Bilirubin was elevated at 1.44mg% with elevated liver enzymes (LDH 2525IU/L, SGOT 206IU/L, SGPT 134IU/L, Alkaline phosphatase 375 IU/L). Her blood sugar random was 88mg%. Her blood group was A+ve. She tested negative for HIV and HBsAg. Urea and creatinine and uric acid were slightly elevated for pregnancy, but returned to normal after hydration with intravenous fluids. When the pretransfusion vitamin B12 and serum folate levels became available they proved to be below the normal range. Her B12 143 pg/ml (nonpregnant range 160-800) however, serum folate was measured on same pretransfusion sample and was found to be abnormally low, at 1 µg/l (nonpregnant range 3.7-14.4). The diagnosis therefore was one of acute megaloblastic anaemia secondary to folate deficiency.

In view of all these laboratory parameters she was transfused with 3 Packed red cells and 4 Fresh frozen Plasma and 2 unit of Random Donor Platelet to build her up prior to induction of labour. She was started on Cap labetalol 250 mg 8 hourly, Inj dexamethsone 10 mg every 12 hourly and Inj MgSO4 as per Prichard regime. Her post transfusion repeat lab reports showed Hb 8.1, TLC 2400cu/mm, Platelet 40000/cumm, Prothrombin time-13 seconds, INR-1.01, however her PIH profile remain unchanged. Then she was induced with cerviprime gel and delivered a healthy female child of 2.4 kg. But unfortunately as was expected she landed up in atonic PPH, which was further controlled with oxytocics and transfusion of 2 Packed red cells and 4 FFP. On 6th day postpartum, laboratory findings were as follows: serum ALT 55 IU/L, serum AST 31 IU/L, serum LDH 267 IU/L, white blood cell 10500/mm, hematocrit 32.8%, hemoglobin 9.4 mg/dl and platelet count 167 x 103/mL. Blood pressure measurement was 130/84 mm Hg. One weeks postpartum, the patient was with no complaint and discharged from the hospital in a stable status.

(Continued on page 290)
Ovarian Tumours in Pregnancy and Puerperium with Notes on Five Cases

Sreelatha Sampath Kumar, Vedavathy Nayak, Prathiba, Ashwini Rani

INTRODUCTION

With the advent of routine prenatal ultrasound, the detection of ovarian mass has become common. Large ovarian cysts that are 5 cm or more are estimated to occur in 0.5-2 per 1000 pregnancies. Torsion of the ovary is the total or partial rotation of the adnexa around its vascular axis or pedicle. Moderate size, free mobility and long pedicle are predisposing factors. Complete torsion causes venous and lymphatic blockade leading to stasis and venous congestion, haemorrhage and necrosis and rupture. Patient usually presents with acute severe pain abdomen and pelvic examination may reveal a tender cystic mass separate from the uterus.

The risk of ovarian torsion rises by 5 fold during pregnancy. Incidence of torsion in pregnancy is 11-12% and in puerperium is 2-3 times this figure, i.e., 23-33%. A couple of mechanical factors predispose to torsion in puerperium. They are lax abdominal musculature and any dynamic, sudden change in the anatomical relations of the pelvic organs. In a recent review of ovarian cysts in pregnancy, if the cysts were noted after 16 weeks of gestation, 20% were functional cysts, 50% were serous cysts, 10% were mucinous cysts and 35% were dermoid cysts. The incidence of malignancy is 1-3%. The majority of ovarian masses detected in first trimester of pregnancy disappear by early second trimester.
Understanding of the benign nature and uncomplicated course of ovarian masses diagnosed incidentally by ultrasound has led to a more conservative but careful and vigilant approach to management of ovarian masses in pregnancy. Emergent surgical intervention is associated with increased risk of adverse outcome for both mother and foetus. Optimal management lies in weighing the risk of expectant management versus intervention in individual cases.

The aim of this study was to review ovarian masses in pregnancy and puerperium that were managed conservatively and if symptomatic with surgery.

Case Reports

Case 1
A 26 years, primigravida presented with 12 weeks of pregnancy and abdominal pain on right side. She was afebrile. Scan showed single live intrauterine pregnancy with an ovarian cyst in the right ovary of 8cm x 6cm. Doppler velocimetry was normal. Patient was managed conservatively with analgesics and progesterone supplementation and was discharged after 3 days. She was regularly followed up antenataly. A scan done at 24 weeks showed regression of the cyst to 6cm x 4 cm. Rest of antenatal period was uneventful. She had a normal vaginal delivery at 39 weeks and the newborn was healthy. Cyst was persisting in the puerperium, was treated with combined estrogen progesterone pill for 3 cycles. Repeat scan showed complete resolution of the cyst.

Case 2
A 30 years, primigravida presented with abdominal pain at 16 weeks of gestation. Ultrasound showed single live intrauterine pregnancy with an ovarian cyst in the right ovary of 8cm x 6cm. Doppler velocimetry was normal. Patient was managed conservatively with analgesics and progesterone supplementation and was discharged after 3 days. She was regularly followed up antenataly. A scan done at 24 weeks showed complete resolution of the ovarian cyst. Rest of antenatal period was uneventful. Patient had a normal vaginal delivery at 38 weeks, the newborn was healthy.

Case 3
A 27 years, second gravida presented at 24 weeks of gestation with abdominal pain. Ultrasound suggested well defined left ovarian cyst of 5cmx5.5 cm with minimal echogenicity. Patient was kept under observation with antibiotics and analgesics. Steroids and progesterone supplementation were given. Patient was discharged after 5 days of conservative treatment. She delivered a healthy baby at term. Follow up scan showed complete resolution of the cyst in the puerperium.

Case 4
A 28 years, second gravida presented at 14 weeks of gestation and mild right abdominal pain. Patient had an ultrasound report which showed a right ovarian clear cyst of 7cmx 5cm. Patient was admitted and managed conservatively with analgesics and progesterone supplementation. Scan done at 26 weeks showed decrease in size of the cyst to 5cm x 4cms. She had a spontaneous vaginal delivery at 39 weeks of gestation and the newborn was healthy. On follow up of the patient in the puerperium, cyst was persisting. Patient was put on 3 cycles of combined estrogen progesterone pill after which scan showed complete resolution of the cyst.

Case 5
A 29 years old, second gravida presented at 18 weeks of pregnancy with abdominal pain. Admission ultrasound showed unilocular, left ovarian cyst with minimal echogenicity without septations measuring 14cmsx12cms. Patient was admitted and
treated conservatively with analgesics. Follow up scans showed persistence of the cyst throughout pregnancy. Patient had a spontaneous vaginal delivery at 39 +4 weeks and the newborn was healthy. As patient was not willing for a laparotomy in the immediate puerperium, she was discharged on the 5th day. Patient came back to the hospital on the 17th postpartum day with acute severe pain abdomen and vomiting. On examination, patient had tachycardia. Abdominal palpation showed tender mass upto 24 weeks gravid uterus size. Ultrasound showed left ovarian cyst 16cmsx14cms. Emergency laparotomy was done in view of suspected torsion. Laparotomy showed left ovarian cyst of 12cmsx10cms with bluish discoloration and with complete torsion. Left oopherectomy was done. Histopathology showed serous cystadenoma. Postoperative period was uneventful.

DISCUSSION

There were five cases of ovarian masses during pregnancy and puerperium in our series. Only one patient required a laparotomy for torsion in the puerperium. Histopathology of the ovarian mass was benign serous cystadenoma. In 2 cases, the cysts regressed in size in the 2nd trimester and resolved completely in the puerperium. In 2 cases, the cysts reduced in size but persisted in the puerperium. They were treated conservatively with low dose estrogen progesterone combination pills for 3 cycles after which they resolved completely.

Incidence of ovarian surgery required in pregnancy is about 1:1312 pregnancies. Torsion of ovary is a dreaded complication leading to infarction, infection, sepsis, peritonitis and adhesions when treatment is delayed. Sixty percent of ovarian torsion occurs between 10-17 weeks of gestation and emergency intervention is needed for all cases of torsion to relieve symptoms.

Abortion is a common complication of abdominal surgery in first trimester. Although second trimester surgery is safe and ideal, it has increased risk of adverse pregnancy outcome like preterm labour hence, surgical management needs to be reconsidered.

Ultrasound is quite accurate for detection and assessment of risk of malignancy. Morphological criteria are more accurate for identification of benign cyst than malignant mass. Ultrasound should be the first imaging modality of investigation for ovarian mass in pregnant or non-pregnant women. MRI can be safely used in pregnancy to evaluate tissue composition and to differentiate ovarian mass from other abdominal mass. Ultrasound for ovarian mass evaluation is technically difficult in third trimester hence MRI is especially useful for third trimester imaging. The clinical significance of CA 125 tumor marker in epithelial ovarian tumor in pregnancy is less, because it is elevated in pregnancy. Expectant management is recommended for most pregnant patients with asymptomatic, non-suspicious cystic ovarian masses. Simple cystic masses that are < 6 cm do not require laparotomy during pregnancy as the risk of malignancy is below 1% and if ovarian
mass persists into the second trimester and it is > 8 cm, rapidly growing or complex mass suspicious of malignancy, surgery should be performed.

CONCLUSION

Ovarian masses are frequently diagnosed during pregnancy. The majority of these are functional or physiological ovarian cysts, which resolve spontaneously by the second trimester. Even among persistent masses, malignancy is rare. Ideal time for scheduled surgery is beginning of second trimester. Carefully selected masses can be followed until term and surgery can be performed during cesarean delivery if they are still present. Given the risk of torsion, rupture, or obstruction, immediate surgery is to be performed irrespective of gestational age, with due risk of abortion or provoked prematurity and fetal morbidity. Although second trimester surgery is safe and ideal, it has increased risk of adverse pregnancy outcome hence, surgical management needs to be reconsidered.

About the Authors

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Management Strategies for Postmenopausal Osteoporosis

INTRODUCTION

Osteoporosis is a chronic, progressive skeletal disorder defined as compromised bone strength and microarchitectural deterioration of bone tissue, that places a patient at risk for bone fragility and fractures, characteristically fractures of the wrist, hip, and spine resulting from minimal trauma (such as a fall from height). Bone strength is made up of two components: bone density and bone quality. Bone density may be measured with dual-energy X-ray absorptiometry (DEXA); it is the basis of the WHO classification of osteopenia and osteoporosis according to which T-scores is summarised in table 1.

Prevalence of Osteoporosis Among Indian Women

Osteoporosis is a major global public health disorder generally leads to considerable morbidity, mortality and socioeconomic burden. It mostly affect women during perimenopause (associated with oestrogen insufficiency). According to expert an group the number of osteoporosis patients in India is approximately 26 million in 2003 and the number is likely to increase up to 36 million by the year 2013.

According to Acharya et al., study osteoporosis and osteopenia are widely prevalent among females of the 40-60 age

Table 1. WHO classification of osteopenia and osteoporosis

<table>
<thead>
<tr>
<th>Classification</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>BMD within 1SD of young normal adult, T-score &gt; 1.0 or higher</td>
</tr>
<tr>
<td>Low bone mass, or osteopenia</td>
<td>BMD between 1 and 2.5 SD lower than that of young normal adult, T-score between -1.0 and -2.5</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>BMD more than 2.5 SD lower than that of young normal adult, T-score &lt; -2.5 or lower</td>
</tr>
</tbody>
</table>

WHO= World Health Organization; DEXA= dual-energy X-ray absorptiometry; BMD= bone mineral density; SD= standard deviation.
groups in India. Average Bone mineral density (BMD) of spine was 0.89gm/cm² and average BMD of hip was 0.85gm/cm² among study population. The correlation between BMD and age was negative. There was a rise in the percentage of population diagnosed as osteoporotic and osteopenia as age increased as shown in figure 1. Spine DEXA was found to be more significant than hip DEXA for osteoporosis assessment.

Pathophysiology and Risk Factors

Bone remodeling is a coupled process of bone resorption followed by bone formation. The major pathophysiology of osteoporosis is an imbalance between bone resorption and bone formation under certain physiological condition. Normal bone formation and remodeling includes constant matrix remodeling of bone. Osteoclasts cells cause bone resorption through stimulation of acid and enzyme production that dissolve mineral and proteins in bone. By this process, new bone is deposited by osteoblast cells by developing a protein matrix consisting of collagen that is soon calcified, resulting in mineralised bone. Osteoporosis is due to increased bone resorption or decreased bone formation or an inadequate formation of new bone. Osteoporosis can be caused by failure in new bone formation and reach peak bone mass as a young adult and by bone loss in older age. Accelerated bone loss can be affected by hormonal status, as occurs in perimenopausal women (associated with lower 17A-oestradiol level, related mainly to the loss of oestrogen-mediated inhibition of bone resorption and this results in the development of fragile bone tissue ultimately increasing the risk of fracture); can impact elderly men and women; and can be secondary to various disease states and medications. Other factors which results in osteoporosis are deficiency of calcium and vitamin D also leads to impaired bone deposition. Parathyroid hormone (PTH) due to low calcium levels also increases bone resorption (Figure 2).

Clinical risk factors associated with osteoporosis are listed below:

- Low calcium or vitamin D intake
- Increasing age
- Low body weight
- Medical history of fracture
- Family history
- White or Asian race

![Figure 1. Women with hip, spine, and total osteoporosis](image1)

![Figure 2. Pathophysiology of osteoporosis](image2)
Impact of Osteoporosis on Quality of Life of Postmenopausal Women

Numerous studies have demonstrated that osteoporosis and the related fractures have significant adverse effects on the health-associated quality-of-life (QoL) of the postmenopausal women. Osteoporosis may affect people at different degrees and extend. Hallberg et al., had conducted a study to assess the impact of osteoporosis fractures on health related QoL in 303 postmenopausal women. The results demonstrated that even after 2 years of hip fracture, health-associated QoL was still below normal regarding physical function, role-physical and social function, while after vertebral fracture. Patients with osteoporosis had lower health-related QoL than those with normal BMD.9

Management of Osteoporosis

Osteoporosis is a condition that can be prevented and treated properly if diagnosed early. Therapy should be individualised based on each patient’s clinical scenario, with the risks and benefits of treatment discussed between the clinician and patient. Exiting management and treatment approaches are summarised in figure 3.

Calcium

Most postmenopausal women consume inadequate amounts of dietary calcium; therefore, supplementation is needed but calcium supplements may cause constipation and gastrointestinal upset. The absorption of numerous medications, most notably levothyroxine, fluoroquinolones, tetracycline, phenytoin, angiotensin-converting enzyme inhibitors, iron, and bisphosphonates, can be significantly decreased when given with calcium.8 These medications should be given several hours before or after calcium supplements. According to Bolland et al., calcium supplementation can also increase the risk of myocardial infarction.10

Vitamin D

Deficiency of vitamin D is associated with suppression in intestinal calcium absorption and the impairment of calcium balance, which results in low bone mineral content and density. Adequate levels of vitamin D maintain bone strength and prevent osteoporosis in older adults, non-ambulatory individuals who have difficulty in exercising, postmenopausal women.11

The National Osteoporosis Foundation (NOF) recommends 800 to 1,000 IU of vitamin D daily for persons 50 years and older. Because it is difficult to consume this amount of dietary vitamin D, supplementation is important.12

For patients with documented vitamin D deficiency, oral ergocalciferol (vitamin D2) in a dosage of 50,000 IU weekly for 8 weeks is usually an effective treatment. This should be followed by a
maintenance dosage of 50,000 IU every 2-4 weeks or oral cholecalciferol (vitamin D₃) in a dosage of 1,000 IU once daily.¹¹

**Bisphosphonates**
Bisphosphonates increase BMD, primarily at the lumbar spine, but also at the proximal femur. In patients who have established osteoporosis, bisphosphonates reduce the risk of vertebral fractures.¹³

**Side effects:** Bisphosphonates irritate oesophagus and are not recommended to patients who cannot remain upright, who have active upper gastrointestinal symptoms, or have delayed oesophageal emptying. One third of patients receiving first IV dose or monthly oral dose of nitrogen-containing bisphosphonate experiences acute-phase reactions (fever, myalgias, lymphopenia).

Renal toxicity may occur with rapid IV administration. It is contraindicated in patients with creatinine clearance less than 30-35 ml/min. With rapid parenteral administration of bisphosphonates, hypocalcemia may occur.¹⁴

**Hormone-related Therapy (HRT)**
It can prevent bone loss in post-menopausal women and reduce fracture risk. However, because HRT has been associated with a relative increase in the incidence of cardiovascular disease (heart attack and stroke) and breast cancer, it is not recommended for long-term use.¹⁵

**Alendronate:** Is a potent HRT but it is associated with inflammatory eye disorders. Report to Centre for Adverse Reactions Monitoring indicates that alendronate may cause synovitis, which can be severe. The risk of oesophagitis and oesophageal ulceration, which may lead to stricture or perforation are observed with alendronate.¹⁶

**Zoledronate:** Acute renal failure requiring dialysis and fatal outcomes have been reported to the FDA following the use of zoledronate. It is contraindicated with moderate to severe renal impairment or in patients with evidence of acute renal impairment.⁵

**Selective Estrogen Receptor Modulator (SERM)**
This class of drugs works in a way that is either similar to or opposite to oestrogen, depending on which organ the drug is acting on. In bone it acts like oestrogen to reduce bone loss. SERM reduces the incidence of spinal fractures by up to 50% but has not been demonstrated to reduce the risk of hip non-spinal fractures. There is an increased risk of clots and fatal stroke. An increased risk of venous thrombosis (clotting), endometrial cancer has been reported with SERM, similar to that seen with HRT. And other side-effects associated with SERMs are as follows:¹⁷

- Abnormal vaginal bleeding or discharge
- Pain or pressure in the pelvis
- Leg edema or tenderness
- Chest pain
- Shortness of breath
- Weakness, tingling, or numbness in your face, arm, or leg
- Sudden difficulty seeing
- Dizziness
- Sudden severe headache

**Raloxifene**
Raloxifene is a SERM that produces both oestrogen-agonistic effects on bone and lipid metabolism and oestrogen-antagonistic effects on uterine endometrium and breast tissue.

**Side effects:** Commonly reported adverse events with raloxifene are hot flushes and leg cramps.
Thromboembolic events such as deep venous thrombosis, pulmonary embolism and retinal vein thrombosis have been reported with raloxifene therapy and are more likely to occur during the first four months of treatment. Because of this potential problem, raloxifene should not be used in women with active venous thromboembolic disease or a history of such disease. Raloxifene should also be avoided in pregnant women.18

**Herbal Treatment**

Medical practitioners are increasingly looking to natural health products to manage osteoporosis and they need evidence-based information on which to base recommendations regarding use and efficacy. The Indian system of medicine mentions several plants that are used to heal fractures and cure many metabolic bone disorders which are as follows:

**Arjuna (Terminalia Arjuna)**

It is extensively used to treat osteoporosis and other bone related disorders as it improves the synthesis and secretion of female hormones. It contains bioactive compounds, which have vitamin D-like action that ensures higher calcium bioavailability.19

**Ashvagandha (Withania Somnifera)**

*W. somnifera* is considered a rejuvenator in Ayurveda. It helps in relieving pain associated with osteoporosis, nervous exhaustion and muscular pains. Withanolides, are extracted from Withania somnifera. They are employed in the treatment of bone related disorders and are potent inhibitors of angiogenesis, inflammation and oxidative stress. Withanolides can also inhibit the activation of NF-kB (gene responsible for arthritic actions). In addition, *W. somnifera* also display potent analgesic and antipyretic effects, without any sign of gastric damage. *W. somnifera* have suppressive effect on osteoporosis by reducing amplification and propagation of the inflammatory response. *W. somnifera* is a rejuvenator that helps in relieving pain associated with osteodystrophic conditions and is also useful in people with general debility, nervous problems and muscular pain.19,20

**Guggulu (Commiphora Wightii)**

*C. wightii* helps in remineralisation of the bones, thus reversing the process of osteoporosis. It possesses analgesic and anti-inflammatory properties, which help relieve bone pain.19

**Bala (Sida Cordifolia)**

It contains phytosterol and potent phytoestrogens. Kanth and Diwan also demonstrated that *S. cordifolia* can increase pain tolerance and appears to have anti-inflammatory properties. Use in aching joints and bones.21

**Godanti and Kukkutandatvak Bhasmas**

Kukkutandatvak bhasma is rich in elemental calcium (CaCO₃), which helps in better bioavailability of calcium. Godanti bhasma provides natural, easily absorbable calcium, and helps to maintain healthy bone structure. Godanti bhasma and kukkutandatvak bhasma are well known for their bone remineralisation properties. Kukkutandatvak bhasma has an additional adaptogenic property, which is useful in relieving general debility in postmenopausal women.19

**Pluchea lanceolata, C. wightii, W. somnifera, S. cordifolia, and Kukkutandatvak bhasma** possess analgesic and anti-inflammatory properties, which help relieve bone pain.19

**SUMMARY**

Osteoporosis is one of the major disorder responsible for postmenopausal women’s morbidity and
mortality and affect their health-associated QoL adversely. The prevention and management of postmenopausal osteoporosis in current medicine system includes oestrogenic therapies, SERMs, bisphosphonates, calcium and vitamin D supplementation. However, the side-effects associated with these drugs, limit their long-term usage and restrict their usage in older patients or patient with other complications. Recently, phytoestrogens (plant derived oestrogens) have been shown to be beneficial in the management of osteoporosis in postmenopausal women. Herbal drugs such as C. wightii, W. somnifera, S. cordifolia, and Kukkuntandav bhasma are rich in phytoestrogens, calcium and vitamin D and thus have bone mineralization properties. They also have analgesic and anti-inflammatory properties contribute to their anti-osteoporotic effect. Herbal therapy generally associated with lesser clinically significant side-effects which reflect the short- and long-term safety and subsequently better compliance to the treatment.

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Case of the Month
A Case of Folate Deficiency
Ashwini Avinash Yelikar, GS Shekhawat, Pushpalatha Naphade

SEVERE FOLATE DEFICIENCY IN PREGNANCY WITH PANCYTOPENIA AND HELLP SYNDROME

The HELLP syndrome and other hypertensive disorders are the main cause of maternal mortality. The HELLP syndrome occurs in about 0.5-0.9% of all pregnancies and in about 10-20% of severe preeclampsia cases. A mild and self limited course to a fulminant process including multiple organ failure can be seen in HELLP syndrome. In most cases, the postpartum HELLP syndrome would resolve spontaneously within 48 hours. Administration of high dose corticosteroid in postpartum period has proved to be helpful for recovery. Haddad et al. showed that adverse maternal outcomes could be seen in 38% of women with HELLP syndrome. These major maternal complications include disseminated intravascular coagulation (DIC), abruptio placenta, acute renal failure pulmonary oedema, and subcapsular liver haematoma.

There have been few case reports of pancytopenia as the result of folate deficiency in pregnancy. The first concerned a patient with severe nausea and vomiting throughout pregnancy (Solano & Councell, 1986). She had a normal haemoglobin concentration at 18 weeks, then presented with pancytopenia at term. She had a low red cell folate level, and was also iron deficient. The second report involved a grand multiparous patient, also with pancytopenia at term (Van der Velde et al., 2002). Both serum and red cell folate levels were low. Pregnancy is associated with a negative folate balance (Chanarin, 1979). Folate is required for growth of the foetus, placenta and maternal tissues, and the foetus actively accumulates reserves. Estimates of dietary requirement in pregnancy are between 600 and 800 mcg/day, whereas the average daily intake in unsupplemented women is invariably low in poor socio economic pregnant patient. Megaloblastic anaemia occurs following 17-19 weeks of negative folate balance. In India 5-10% of pregnant women, not receiving folate supplementation have been found to have megaloblastic anaemia. Pregnant women with a megaloblastic marrow because of folate deficiency may also be iron deficient, resulting in a normal mean red cell volume. There is considerable overlap in the range of serum folate concentrations in pregnant women with normal haemopoiesis and those with megaloblastic anaemia, and 40% of the latter have serum folate levels within the normal range for pregnancy. Red cell folate does not vary in the short-term and is a better reflection of tissue stores.

Folate supplementation for the prevention of neural tube defects is recommended for all women planning a pregnancy, beginning prior to pregnancy and continuing until 12 weeks gestation. The recommended dose is 400 mcg daily, and 5 mg daily for women at high risk (previously affected foetus, family history, folate-antagonist drugs such as anti-epileptics). However, many women are at risk of clinical sequelae because of folate deficiency in pregnancy, and supplementation may be necessary. Pregnant women with dietary iron deficiency may also have co-existing folate deficiency, and consideration should be given to concomitant folate supplementation. Increased red cell production because of treatment of severe iron deficiency may deplete body folate stores, resulting in severe megaloblastic anaemia.

In summary, folate deficiency is common in pregnancy and may not be apparent. We propose that consideration be given to folate supplementation for all women throughout pregnancy in order to avoid not only neural tube defects but also dreadful complications like HELLP syndrome to further reduce the associated maternal mortality.

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The complete list of references is available on request to the editorial office.
Clinical Study of HELLP Syndrome in Hypertensive Disorders of Pregnancy

Gadappa Shrinivas, Sonali Deshpande, Kanan Yelikar

INTRODUCTION

Haemolysis, elevated liver enzymes and low platelets count has been recognized as a complication of preeclampsia- eclampsia for decades. In 1982, Weinstein described 29 cases of severe preeclampsia complicated by thrombocytopenia, abnormal peripheral blood smear and abnormal liver functions test and is credited with coining the acronym ‘HELLP syndrome’ into the obstetric vernacular. During ensuing two decades, two large series from the Universities of Tennesee and Mississippi further characterized HELLP syndrome as a form of severe preeclampsia with the potential to cause critical illness and death during perinatal period. Though the syndrome has been considered a variant of preeclampsia, it can occur on its own or in association with preeclampsia.

Since 1982, there has been an outpouring of obstetric literature seeking better to define the pathogenesis, natural history, clinical spectrum, classification and management strategies for women considered to have HELLP syndrome and hence there was a need for an in depth studies of the incidence, pathogenesis, symptomatology and management of HELLP syndrome.

In the present study, the focus rests on classification of HELLP syndrome as complete or partial. The idea was to study the trend of investigations i.e. platelets, liver function tests and serum LDH and the maternal and perinatal outcome for a better understanding of this obstetric challenge.

Aims and Objective of the Study

- To study the incidence of HELLP syndrome
- To study the spectrum of HELLP syndrome.
- To study the maternal and perinatal outcome of HELLP syndrome.

Material and Methods

- **Design:** Prospective observational study.
- **Number of women:** 128
- **Duration of study period:** January 2009 - December 2011.

**Inclusion Criteria**

All laboratory diagnosed cases of HELLP Syndrome were included in the study.

**Exclusion Criteria**

Thrombotic thrombocytopenic purpura, Haemolytic uremic syndrome, immune thrombocytopenic purpura. Acute fatty liver of pregnancy, SLE antiphospholipid syndrome, cholecystitis, fulminant viral hepatitis, acute pancreatitis disseminated herpes simplex.

After admission, detailed personal and socio-demographic history was obtained. Chief complaints enlisted including leading questions regarding the complications in terms of symptomatology such
as headache, nausea, vomiting, blurring of vision, upper abdominal pain, history of preeclampsia/HELLP syndrome in previous pregnancies, its maternal and foetal outcome was also elicited. General and systemic examination was carried out then following investigations were carried out on D1 and repeated on D3 and if required on D5; CBC, urine, blood grouping and Rh typing, bleeding time, clotting time, coagulation profile, LFTs, KFTs and fundus examination, USG.

After investigations mother was classified according to Tennessee classification into complete/partial HELLP

- **Complete HELLP**: Platelets < 1,00,000/ Ul, LDH > 600 IU/L, AST > 70 IU / L

- **Partial HELLP**: Only one or two of these criteria’s present.

The maternal condition was assessed and stabilised by controlling hypertension with Tab./Inj. Labetalol if systolic B.P more than 160 mm of Hg and/or diastolic B.P is more than 110 mm of Hg as per the requirement, convulsion prophylaxis with magnesium sulphate and correction of coagulopathy if DIC was present. Evaluation of foetal well-being was done with the help of NST and USG. Based on the severity, mother was classified as complete/partial HELLP Syndrome.

The administration of corticosteroids to the mother was done to enhance foetal lung maturity and to ameliorate the disease process.

**Ante partum**: 10 mg dexamethasone was given intravenously every 12 hourly. For selected patients at highest risk, including cases of profound thrombocytopenia and CNS dysfunction: 20 mg intravenous dexamethasone was given 12 hourly for 4 doses.

**Postpartum**: 10 mg intravenous dexamethasone was continued 12 hourly till
- Maternal platelet count was >1, 00,000 cu/mm
- LDH levels showed a decreasing trend.
- Urine output improved to > 100 ml/hour and then 5 mg intravenous dexamethasone was given 12 hourly for 2 doses.

Vaginal trial was given depending on status of cervical dilatation and its inducibility. Caesarean section was performed for obstetric indication. Spectrum of the disease was noted and maternal and perinatal outcome was noted. Woman

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Women with complete HELLP syndrome (n=40)</th>
<th>Women with partial HELLP syndrome (n=88)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age</td>
<td>24.6±3.48</td>
<td>25±2.82</td>
</tr>
<tr>
<td>Range</td>
<td>18-35 years</td>
<td>18-35 years</td>
</tr>
<tr>
<td>Gravidity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G1</td>
<td>25(62.5%)</td>
<td>41(46.5%)</td>
</tr>
<tr>
<td>G2-4</td>
<td>10(25%)</td>
<td>35(39.8%)</td>
</tr>
<tr>
<td>G&gt;4</td>
<td>5(12.5%)</td>
<td>12(13.6%)</td>
</tr>
<tr>
<td>ANC Registration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Booked</td>
<td>9(22.5%)</td>
<td>74(83.09%)</td>
</tr>
<tr>
<td>Unbooked</td>
<td>31(77.5%)</td>
<td>14(15.90%)</td>
</tr>
<tr>
<td>Residence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>22(55%)</td>
<td>57(65.1%)</td>
</tr>
<tr>
<td>Rural</td>
<td>18(45%)</td>
<td>31(35.22%)</td>
</tr>
<tr>
<td>Gestational age in weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 28</td>
<td>18(45%)</td>
<td>20(22.7%)</td>
</tr>
<tr>
<td>29 – 36</td>
<td>15(37.5%)</td>
<td>30(34.1%)</td>
</tr>
<tr>
<td>&gt;36</td>
<td>7(3.9%)</td>
<td>38(43.2%)</td>
</tr>
<tr>
<td>Proteinuria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>trace</td>
<td>-</td>
<td>19(21.5%)</td>
</tr>
<tr>
<td>1+</td>
<td>2(5%)</td>
<td>21(23.8%)</td>
</tr>
<tr>
<td>2+</td>
<td>5(12.5%)</td>
<td>15(17%)</td>
</tr>
<tr>
<td>&gt;2+</td>
<td>33(82.5%)</td>
<td>33(37.5%)</td>
</tr>
<tr>
<td>Systolic B.P. in mm of Hg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;140</td>
<td>10(25%)</td>
<td>40(45.45)</td>
</tr>
<tr>
<td>140-160</td>
<td>20(50%)</td>
<td>35(39.77%)</td>
</tr>
<tr>
<td>161-180</td>
<td>8(20%)</td>
<td>12(13.63%)</td>
</tr>
<tr>
<td>&gt;180</td>
<td>2(5%)</td>
<td>1(1.1%)</td>
</tr>
<tr>
<td>Diastolic B.P. in mm of Hg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>90-110</td>
<td>15(37.5%)</td>
<td>50(56.8%)</td>
</tr>
<tr>
<td>&gt;110</td>
<td>25(62.5%)</td>
<td>38(43.1%)</td>
</tr>
</tbody>
</table>
was discharged only after improvement in general condition.

RESULTS

Incidence of HELLP syndrome was 4.5/1000 deliveries and 68/1000 in hypertensive disorders of pregnancy.

Table I shows the socio-demographic and clinical characteristics of the 128 women enrolled in study.

Table II shows the symptomatology of women suffering from HELLP syndrome. Headache was the most common symptom followed by epigastric pain, nausea and vomiting and there incidence in partial and complete HELLP syndrome are 75% and 23.43%, 75% and 28.40%, 62.5% and 22.72% respectively. All women with complete HELLP syndrome were symptomatic while 18.1% women were asymptomatic in partial HELLP syndrome.

Table III shows laboratory trend of investigation in complete and partial HELLP syndrome on D1, D3 and D5 and mean values of platelet count, LDH and AST. Complete HELLP syndrome is a severe form of disease spectrum with higher derangement in laboratory values when compared with the entity of partial HELLP syndrome and showing improvement in investigation after delivery due to the relieved vasoconstriction leading to reversal of liver ischaemia.

Table IV shows distribution of cases of partial HELLP syndrome as per the derangement of one or two laboratory investigations. 62.5% women had raised LDH followed by 23.86% had raised LDH and low platelet count. 1.13% women had only low platelet count.

Table V shows maternal outcome, 92.5% of women with complete HELLP and 94.31% of women with partial HELLP syndrome delivered vaginally whereas 7.5% and 5.68% respectively required operative interference. Serious maternal complications were noted in the form of blood product transfusion in 87.5% and 11.4% of women with complete and partial HELLP syndrome respectively followed by Abruptio (10% and 11.45%), DIC (35% and 3.4%), ARF (12.5% and 2.26%), Pulmonary oedema (10% and 2.26) and CVA (7.5% and 1.13%). Maternal mortality was noted in 2(5%) women suffering from complete HELLP syndrome, reason being pulmonary edema and CVA. There is no mortality in partial HELLP syndrome.

Table VI: shows perinatal outcome, out of 50(39.06%) babies who were healthy and shifted with mothers, 45(90%) were born to mothers suffering from partial HELLP syndrome. Out of 40(31.25%) babies who were still born, 19(47.5%) were born to mothers suffering from complete HELLP syndrome. 16(40%) babies of women with complete HELLP syndrome and 22(25%) babies of women with partial HELLP syndrome were admitted in NICU.

Table 2. Symptomatology in women with HELLP syndrome

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>HELLP syndrome</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Complete HELLP (n=40)</td>
<td>Partial HELLP syndrome (n=88)</td>
</tr>
<tr>
<td>Headache</td>
<td>30 (75%)</td>
<td>30 (23.43%)</td>
</tr>
<tr>
<td>Epigastric Pain</td>
<td>30 (75%)</td>
<td>25 (28.40%)</td>
</tr>
<tr>
<td>Nausea and Vomiting</td>
<td>25 (62.5%)</td>
<td>20 (22.72%)</td>
</tr>
<tr>
<td>Malaise</td>
<td>03 (7.5%)</td>
<td>04 (3.12%)</td>
</tr>
<tr>
<td>Oliguria</td>
<td>05 (12.5%)</td>
<td>02 (2.26%)</td>
</tr>
<tr>
<td>Visual symptoms</td>
<td>02 (5%)</td>
<td>03 (3.4%)</td>
</tr>
<tr>
<td>No symptoms</td>
<td>-</td>
<td>16 (18.1%)</td>
</tr>
</tbody>
</table>

Table 3. Laboratory investigation trend

<table>
<thead>
<tr>
<th>HELLP syndrome</th>
<th>Investigations (Mean Values)</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>D1</td>
</tr>
<tr>
<td>Complete</td>
<td>Platelet count (/Cumm)</td>
<td>45,000</td>
</tr>
<tr>
<td></td>
<td>LDH (IU/L)</td>
<td>1000</td>
</tr>
<tr>
<td></td>
<td>AST (IU/L)</td>
<td>225</td>
</tr>
<tr>
<td>Partial</td>
<td>Platelet count (/Cumm)</td>
<td>80,000</td>
</tr>
<tr>
<td></td>
<td>LDH (IU/L)</td>
<td>700</td>
</tr>
<tr>
<td></td>
<td>AST (IU/L)</td>
<td>147</td>
</tr>
</tbody>
</table>
HELLP syndrome is a variant of pre-eclampsia associated with high maternal and perinatal morbidity and mortality. It has aptly been quoted that the patient and obstetrician both ask for ‘Help’ in HELLP syndrome. The incidence of HELLP syndrome in present series was found to be 4.5% which was consistent with Kaur Amrit Pal et al.5

Mean age in our study was 24.8 years which was consistent with Kaur Amrit Pal et al.,2 who reported mean age to be 24.2 years and Sibai et al.,3 who reported it to be 25 years. Though the literature describes HELLP syndrome as being a disorder of the multiparas, our study showed 51.56% primigravidas and 48.43% multigravidas. This finding was consistent with Amrit Kaur et al.5

Mean gestational age in present study was 31.18 weeks. 45% women with complete HELLP were diagnosed before 28 weeks of gestation whereas 43.2% women with partial HELLP were having gestational age more than 36 weeks at the time of diagnosis. This finding was consistent with Haddad et al.2 In present series around 62.5% women with complete HELLP and 43.18% women with partial HELLP syndrome were presented with the above mentioned symptom. But 18.1% women with partial HELLP syndrome were not presented with any of these symptoms and diagnosed only by doing investigations. Hence careful examination and relevant investigations are of immense importance in the management of patients.

Table 4. Distribution according to laboratory parameters in partial HELLP

<table>
<thead>
<tr>
<th>Laboratory parameter</th>
<th>Partial HELLP (n=88)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low platelet count</td>
<td>01(1.13%)</td>
</tr>
<tr>
<td>Raised LDH</td>
<td>55(62.5%)</td>
</tr>
<tr>
<td>Raised AST</td>
<td>06(6.8%)</td>
</tr>
<tr>
<td>Low platelet + Raised LDH</td>
<td>21(23.86%)</td>
</tr>
<tr>
<td>Raised LDH + Raised AST</td>
<td>04(4.54%)</td>
</tr>
<tr>
<td>Low platelet + Raised AST</td>
<td>01(1.13%)</td>
</tr>
</tbody>
</table>

Table 5. Maternal outcome

<table>
<thead>
<tr>
<th>Variable</th>
<th>HELLP syndrome</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Complete HELLP</td>
<td>Partial HELLP</td>
</tr>
<tr>
<td></td>
<td>(n=40)</td>
<td>(n=88)</td>
</tr>
<tr>
<td>Mode of Delivery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal</td>
<td>36(90%)</td>
<td>68(77.27%)</td>
</tr>
<tr>
<td>Instrumental</td>
<td>1(2.5%)</td>
<td>15(17.04%)</td>
</tr>
<tr>
<td>LSCS</td>
<td>3(7.5%)</td>
<td>5(5.68%)</td>
</tr>
<tr>
<td>Serious Maternal Complication</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DIC</td>
<td>14(35%)</td>
<td>3(3.40%)</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>5(12.5%)</td>
<td>2(2.26%)</td>
</tr>
<tr>
<td>Pulmonary oedema</td>
<td>4(10%)</td>
<td>2(2.26%)</td>
</tr>
<tr>
<td>Abruption</td>
<td>4(10%)</td>
<td>10(11.4%)</td>
</tr>
<tr>
<td>CVA</td>
<td>3(7.50%)</td>
<td>1(1.13%)</td>
</tr>
<tr>
<td>Blood product transfusion</td>
<td>35(87.5%)</td>
<td>10(11.4%)</td>
</tr>
<tr>
<td>Reason of Maternal Mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary oedema</td>
<td>1(2.5%)</td>
<td>-</td>
</tr>
<tr>
<td>CVA</td>
<td>1(2.5%)</td>
<td>-</td>
</tr>
</tbody>
</table>

epigastric pain, nausea, malaise are the common symptoms in HELLP syndrome. Sibai et al.,3 recommends that all pregnant women displaying any of these symptoms have complete CBC, platelet count and liver function tests irrespective of maternal blood pressure. In present series, all women with complete HELLP syndrome were presented with the above mentioned symptom.
Majority of the women in present study had recovery on postpartum D5 and this finding was consistent with Amrit Pal kaur et al.\textsuperscript{5} This confirms that HELLP syndrome does not cause any permanent damage to hepatic function.

In present study, raised LDH values emerge as the single most commonly deranged parameter in partial HELLP syndrome and this finding was also reported by Francisco Abbade et al.\textsuperscript{7} Women with HELLP syndrome were at increased risk of adverse maternal outcome. Various complications observed in the present study included DIC, ARF, abruption, pulmonary oedema, CVA. However we did not encounter any complication like hepatic rupture, retinal detachment. Shafika Banoo et al\textsuperscript{4} and Audibert F et al.,\textsuperscript{1} also reported these complications. Weinstein et al\textsuperscript{6} reported maternal mortality figures of 4-25% depending on the severity of the disease. In present series maternal mortality was 5% and that too in women with complete HELLP syndrome. Reported perinatal mortality was 8-60%. In present series it was observed to be 47.5% in complete and 14.77% in partial HELLP syndrome.

**CONCLUSION**

Pregnancies complicated by HELLP syndrome are prone to adverse maternal and perinatal outcome; hence all patients of pre-eclampsia should be strictly evaluated for diagnosis of HELLP syndrome for better maternal and fetal outcome. Proper use of component transfusion and judicious termination of pregnancy is mainstay of treatment for safe motherhood.

**About the Authors**

Dr Gadappa Shrinivas is a Associate Professor and Unit Head, Dr Sonali Deshpande is a Associate Professor and Dr Kanana Yelikar is a Professor and HOD, Department Obstetrics and Gynecology, GMC Aurangabad.

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**REFERENCES**


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**Table 6. Perinatal outcome**

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>HELLP syndrome</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Complete HELLP (n=40)</td>
<td>Partial HELLP syndrome (n=88)</td>
</tr>
<tr>
<td>Healthy baby</td>
<td>5 (12.5%)</td>
<td>45 (51.13%)</td>
</tr>
<tr>
<td>Still birth</td>
<td>19 (47.5%)</td>
<td>21 (14.77%)</td>
</tr>
<tr>
<td>NICU Admission</td>
<td>16 (40%)</td>
<td>22 (25%)</td>
</tr>
<tr>
<td>Mean birth weight (kgs)</td>
<td>2.2±3</td>
<td>2.6±4</td>
</tr>
</tbody>
</table>
Cerebroplacental Ratio as a Predictor of Perinatal Outcome in Growth Restricted Foetuses

Shalini Rajaram, Rachna Agarwal, Tuleeka Sethi, Neerja Goel

INTRODUCTION

Doppler interrogation of foetal arteries has provided a useful window for assessing the function of foetal organ systems and is a reliable predictor of placental dysfunction. Umbilical artery (UA) doppler velocimetry is the most sensitive ultrasound parameter in the prenatal diagnosis of intrauterine growth restriction (IUGR) and neonatal outcome. However UA doppler provides insufficient information to solely direct the perinatal management and dictate timing of delivery. In addition, studies have shown that the presence of abnormal doppler waveform in middle cerebral artery (MCA) is associated with an increased likelihood of neonatal compromise and need of delivery.

This study was undertaken to evaluate the umbilical and cerebral circulation in IUGR cases and further evaluate the Cerebral Placental Resistance Index Ratio (CPRIR) for prediction of perinatal morbidity and mortality.

Material and Methods

A prospective, non-randomized study was conducted in the Department of Obstetrics and Gynaecology, University College of Medical Sciences and GTB Hospital. A total of 80 pregnant women were evaluated, study group comprising of 50 pregnant women with IUGR (detailed below) with gestational age >28 weeks and control group of 30 pregnant women with normal growth parameters.

IUGR Criteria

All patients with accurately dated singleton pregnancy of gestational age more than 28 weeks and a discrepancy of more than 4 weeks on clinical examination or 4 cm by symphysio-fundal height and with

<table>
<thead>
<tr>
<th>Perinatal outcome</th>
<th>IUGR group (n = 50)</th>
<th>Control group (n = 30)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live birth</td>
<td>48 (96%)</td>
<td>30 (100%)</td>
<td>0.525 (NS)</td>
</tr>
<tr>
<td>still birth</td>
<td>2 (4%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>neonatal death</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Mean gestational age at delivery</td>
<td>37.4 ± 1.163 weeks</td>
<td>38.5 ± 0.843 weeks</td>
<td>0.671 (NS)</td>
</tr>
<tr>
<td>Mean birth weight (kg)</td>
<td>2.117 ± 0.323</td>
<td>2.817 ± 0.842</td>
<td>0.000 (Sig.)</td>
</tr>
<tr>
<td>Apgar &lt; 7 at 1 min</td>
<td>15 (30%)</td>
<td>2 (6.6%)</td>
<td>0.013 (Sig.)</td>
</tr>
<tr>
<td>NICU admission</td>
<td>16 (32%)</td>
<td>3 (10%)</td>
<td>0.025 (Sig.)</td>
</tr>
<tr>
<td>MSL</td>
<td>9 (18%)</td>
<td>2 (6.6%)</td>
<td>0.194 (NS)</td>
</tr>
<tr>
<td>Normal liquor</td>
<td>41 (82%)</td>
<td>28 (93.4%)</td>
<td></td>
</tr>
</tbody>
</table>

Abbrevations: NS- nonsignificant; Sig.- Significant.
one or more of the following ultrasound findings were included in the study group:

- Abdominal circumference less than 2 SD from mean value or a difference of more than 4 weeks.
- Amniotic fluid index less than 8 cm.
- Femur length to abdominal circumference (FL / AC) ratio more than 24.

**Methodology**

A detailed history and physical examination of the patient was done. Each patient was then subjected to ultrasound examination and Doppler flow studies of umbilical and middle cerebral arteries. Doppler flow examination was performed using Wipro GE LogicTM 500 ultrasound machine with Doppler capability and frequency ranging from 3.5-4 MHz.

The Doppler evaluations were performed at the time of recruitment i.e. at a gestational age between 28 and 34 weeks followed by a second examination between 34 and 38 weeks. The UA and MCA Doppler velocimetric evaluation was done (Figure 1 and 2) and the following indices were calculated: Pulsatility index or PI; Resistance index or RI; Systolic/Diastolic or S/D ratio; and Cerebral Placental Resistance Index Ratio, CPR. CPR was calculated as a ratio of middle cerebral and umbilical artery Resistance index.5,6

The above parameters were then correlated with the perinatal outcome for which the following parameters were recorded - live or still birth, gestational age at delivery, birth weight, meconium stained liquor (MSL), Apgar score at 1 and 5 minutes.

---

**Case Study**

- Figure 1. a) Doppler ultrasonography showing the umbilical artery - flow velocity waveform. b) Doppler ultrasonography showing the middle cerebral artery - flow velocity waveform.
- Figure 2. a) Color Doppler examination and flow velocity waveform of the umbilical artery showing reduced flow at 35 weeks. b) Color Doppler examination and flow velocity waveform of the middle cerebral artery at 35 weeks.
5 minutes and neonatal intensive care unit (NICU) admission. Statistical evaluation was done by repeated measures ANOVA and multiple comparisons. Within the group time points were obtained by Tukey's test at 5% level of significance.

RESULTS

Perinatal outcome was compared in both study and control groups and the data is tabulated in Table 1. The table shows that the Control group (No IUGR) had better Apgar score, higher birth weight and significantly lower admissions to NICU as compared to the Study Group (IUGR).

**Correlation of Doppler Indices with Perinatal Outcome**

We observed that PI, RI and S/D ratio of UA was significantly higher in neonatal death and still birth group than the live birth group (Table 2). The mean PI of the MCA was higher in live birth group than in the still birth group. However, in 1 case of neonatal death, the PI of the MCA artery was much higher.

**Correlation of Doppler Indices with Birth Weight**

On correlating the Doppler flow indices with the birth weight (Table 3) the following inferences could be drawn. There was a significant increase in all doppler resistance indices of umbilical artery

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**Table 2. Correlation of doppler flow indices at 34 to 38 weeks of gestation (2nd visit) with perinatal outcome in IUGR cases**

<table>
<thead>
<tr>
<th>IUGR cases</th>
<th>Live birth</th>
<th>Still birth</th>
<th>Neonatal death</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>47</td>
<td>2</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Umbilical artery PI</td>
<td>1.241 ± 0.968</td>
<td>3.55 ± 2.333</td>
<td>4.410</td>
<td>0.000 (Sig.)</td>
</tr>
<tr>
<td>RI</td>
<td>0.667 ± 0.157</td>
<td>1.37 ± 0.342</td>
<td>1.000</td>
<td>0.000 (Sig.)</td>
</tr>
<tr>
<td>S/D ratio</td>
<td>2.734 ± 0.622</td>
<td>REDV</td>
<td>REDV</td>
<td>1 (NS)</td>
</tr>
<tr>
<td>Middle cerebral artery PI</td>
<td>1.431 ± 0.274</td>
<td>1.150 ± 0.297</td>
<td>1.230</td>
<td>0.515</td>
</tr>
<tr>
<td>RI</td>
<td>0.714 ± 0.127</td>
<td>0.665 ± 0.106</td>
<td>0.690</td>
<td>0.676 (NS)</td>
</tr>
<tr>
<td>S/D ratio</td>
<td>3.575 ± 0.866</td>
<td>3.185 ± 1.053</td>
<td>3.260</td>
<td>0.779 (NS)</td>
</tr>
</tbody>
</table>

*Live birth babies in utero showed lower UA indices versus perinatal death group while MCA pattern showed a differential feature of still birth (MCA PI low) versus neonatal death (MCA PI High). *MCA pattern with low PI, RI, S/D shows brain sparing effect and high PI, RI, S/D shows loss of compensatory mechanism.

---

**Table 3. Correlation of umbilical and middle cerebral artery doppler flow indices at 34 to 38 weeks of gestation (2nd visit) with birth weight in cases (IUGR)**

<table>
<thead>
<tr>
<th>IUGR group</th>
<th>PI</th>
<th>R</th>
<th>S/D Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight</td>
<td>n</td>
<td>UA</td>
<td>MCA</td>
</tr>
<tr>
<td>Less than 1.5 kg</td>
<td>2</td>
<td>3.62 ± 1.12</td>
<td>1.13 ± 0.14</td>
</tr>
<tr>
<td>1.5 to 1.99 kg</td>
<td>1</td>
<td>1.79 ± 1.78</td>
<td>1.35 ± 0.29</td>
</tr>
<tr>
<td>2 to 2.5 kg</td>
<td>3</td>
<td>1.16 ± 0.77</td>
<td>1.45 ± 0.39</td>
</tr>
<tr>
<td>p-value</td>
<td>0.005 (Sig.)</td>
<td>0.399 (NS)</td>
<td>0.001 (Sig.)</td>
</tr>
</tbody>
</table>

| Data in Mean ± S.D. |
as severity of IUGR increased. Thus an inverse correlation exists between umbilical vascular resistance and birth weight as seen in IUGR cases.

MCA flow studies depicted that as severity of IUGR increases the MCA flow pattern shows a decrease in value of all indices i.e. PI, RI and S/D ratio.

**Foetal Vascular Response in Cases of Perinatal Death**

In IUGR group the perinatal outcome was 47 live births, 2 still births and 1 neonatal death (Table 4). The two cases that had still birth developed absent end diastolic flow (AEDF) and reversed end diastolic flow (REDF) respectively in the UA. MCA flow pattern showed a decrease in Doppler flow indices (Brain sparing effect, Figure 3) in the AEDF case, while the REDF case showed a rise in MCA Doppler indices (loss of compensatory effect). The case of neonatal death initially developed AEDF at 33 weeks, which deteriorated to a REDF after 1 week. This patient underwent cesarean section on the same day at 34 weeks of gestation and delivered an extremely low birth weight baby of weight 1 kg with low Apgar of 6 at 1 minute. Neonatal death occurred on the same day.

**Correlation of Doppler Indices with MSL and Apgar score**

The IUGR cases that had MSL had higher umbilical resistance indices than those cases with normal liquor (Table 5). S/D Ratio of UA is higher in those fetuses that had Apgar < 7 than those who had Apgar > 7 at 5 minutes.

**Correlation of Doppler Indices with NICU Admission**

UA Doppler indices were higher in those babies that needed NICU admission than those who were at mother’s side (Table 6). Similarly the middle cerebral flow pattern showed resistance to flow (↑PI and S/D ratio) in cases that needed NICU admission than those who did not (Table 7).

**Study of CPR in IUGR Cases**

The CPR was also assessed and correlated with the various parameters and the data is presented in Table 8. There was a significant decrease in the CPR as the...
birth weight decreased, being lowest in less than 1.5 kg group and highest in 2 to 2.5 kg group. CPR was more than one in live birth group and less than one in those with still births and neonatal death (P = 0.038). Out of eleven babies who had birth weight between 1.5 to 1.9 kg, six had CPR less than one, out of which five were admitted to NICU for variable period of time and one had stillbirth. Both the babies with weight less than 1.5 kg had CPR less than one and were also admitted to NICU.

**DISCUSSION**

The assessment of foetal growth, development and health are considered standard care. Surveillance has been applied to pregnancies complicated by IUGR to improve foetal outcome. Conceptually the application of Doppler allows an assessment of immediate foetal condition and institution of appropriate longitudinal management.

Foetal deterioration of Doppler and Biophysical variables progresses in different time frames. Arterial Doppler changes precede compromises by weeks while changes in amniotic fluid volume, abnormal venous Doppler and decline in foetal breathing, tone and movement occur over progressively shorter periods. The integration of multi vessel Doppler allows for detection of multiple patterns of placental insufficiency and foetal compromise.

Studies by Hecher and Ferrazzi suggest that only 50% of foetuses with abnormal CTG may develop abnormal venous indices while the arterial doppler abnormalities identify a prodrome of foetal disease when the decline in biophysical variables is subtle and predominantly evident on computerised analysis.

Table 6. Correlation of umbilical artery doppler flow indices at different gestational ages with neonatal intensive care unit (NICU) stay in cases (IUGR)

<table>
<thead>
<tr>
<th>Neonatal outcome</th>
<th>PI of umbilical artery</th>
<th>RI of umbilical artery</th>
<th>S/D ratio of umbilical artery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1st visit##</td>
<td>2nd visit</td>
<td>1st visit</td>
</tr>
<tr>
<td>Mother side$</td>
<td>33</td>
<td>1.075 ± 0.231</td>
<td>1.225 ± 0.816</td>
</tr>
<tr>
<td>NICU stay</td>
<td>17</td>
<td>1.588 ± 1.238</td>
<td>1.732 ± 1.655</td>
</tr>
<tr>
<td>p-value</td>
<td>0.024 (Sig.)</td>
<td>0.151 (NS)</td>
<td>0.012 (Sig.)</td>
</tr>
</tbody>
</table>

Data in mean ± S.D.

## 1st visit was conducted at 28 weeks to 34 weeks & 2nd visit was conducted at 34 to 40 weeks of gestation.

$ In two patients of mother side group and three patients of NICU group, S/D ratio was not recordable due to AEDV/REDV.
Pathogenesis of IUGR and Changes in UA and MCA Doppler Indices

In the vast majority of cases of IUGR the underlying defect is the result of poor trophoblastic invasion of maternal spiral arteries and reduced uteroplacental flow. This reduction in intervillus flow results in local, intraplacental stem vessel vasoconstriction to minimise intervillus/intravillus flow mismatch; deleterious shunting is thereby initially prevented and foetal oxygenation maintained. Progressive reduction in intervillus flow would result in progressive foetoplacental vasoconstriction and worsening of the UA Doppler indices. In IUGR cases there is a placental dysfunction which results in umbilical blood flow resistance shown by increase in S/D ratio on Doppler. When this is progressive it is associated with changes in foetal circulation. There is preferential distribution of well oxygenated blood from ductus venosus to the brain, heart and upper body.12

The proportional shift of blood flow towards heart in IUGR, i.e. the centralization of blood flow, may initially be detect-

Table 7. Correlation of middle cerebral artery doppler flow indices at different gestational ages with neonatal intensive care unit (NICU) stay in cases (IUGR)

<table>
<thead>
<tr>
<th>Neonatal outcome</th>
<th>PI of middle cerebral artery</th>
<th>RI of middle cerebral artery</th>
<th>S/D ratio of middle cerebral artery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1st visit##</td>
<td>2nd visit</td>
<td>1st visit</td>
</tr>
<tr>
<td>Mother side</td>
<td>33</td>
<td>1.380 ± 0.412</td>
<td>1.391 ± 0.421</td>
</tr>
<tr>
<td>NIC ustay</td>
<td>17</td>
<td>1.682 ± 0.676</td>
<td>1.465 ± 0.248</td>
</tr>
<tr>
<td>p-value</td>
<td>0.055 (NS)</td>
<td>0.989 (NS)</td>
<td>0.217 (NS)</td>
</tr>
</tbody>
</table>

Data in Mean ± S.D.

## 1st Visit was conducted at 28 weeks to 34 weeks & 2nd visit was conducted at 34 to 40 weeks of gestation.

Table 8. Correlation of CPR with perinatal outcome in IUGR cases

<table>
<thead>
<tr>
<th>Birth weight^</th>
<th>n</th>
<th>CPR 34 - 40 weeks mean ± S.D.</th>
<th>Perinatal outcome</th>
<th>n</th>
<th>CPR 34 - 40 weeks mean ± S.D.</th>
<th>Liquor</th>
<th>n</th>
<th>CPR 34 - 40 weeks mean ± S.D.</th>
<th>NICU Stay</th>
<th>n</th>
<th>CPR 34 - 40 weeks mean ± S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 to 2.5 Kg</td>
<td>37</td>
<td>1.18 ± 0.41</td>
<td>Live Birth</td>
<td>47</td>
<td>1.137 ± 0.380</td>
<td>Normal Liquor</td>
<td>41</td>
<td>1.121 ± 0.403</td>
<td>Mother Side</td>
<td>33</td>
<td>1.132 ± 0.444</td>
</tr>
<tr>
<td>1.5 to 1.99 kg</td>
<td>11</td>
<td>0.94 ± 0.24</td>
<td>Still Birth^▲</td>
<td>2</td>
<td>0.484 ± 0.063</td>
<td>MSL</td>
<td>9</td>
<td>1.033 ± 0.396</td>
<td>NICU Stay</td>
<td>17</td>
<td>1.046 ± 0.284</td>
</tr>
<tr>
<td>Less than 1.5 Kg</td>
<td>2</td>
<td>0.60 ± 0.13</td>
<td>Neonatal Death^▲</td>
<td>1</td>
<td>0.69</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

p-value 0.032 (Sig.) 0.038 (Sig.) 0.557 (NS) 0.476 (NS)

^CPR ↓as birth weight ↓ and CPR <1 in birth weight <2 kg.

^^CPR <1 (perinatal death) vs. CPR >1(live birth).
able by changes in the ratio of MCA to UA Resistance Index, also called the Cerebral Placental Resistance Index Ratio or CPR. CPR measures the proportion of blood flow to the foetal brain and placenta and is more than one in normal pregnancy. A CPR of less than 1 predicts a poor neonatal outcome and identifies a subgroup of patients at high risk for neonatal morbidity and mortality.6,13

**Umbilical Artery –Birth Weight**
We found a significant increase in the UA S/D Ratio with decrease in birth weight, being highest in less than 1.5 kg group and lowest in 2-2.5 kg group in both the visits. Hugo et al., followed 572 singleton pregnancies and found that significantly more infants were SGA when umbilical artery RI was more than 95th percentile and was associated with higher perinatal mortality rate.14 Baschat et al., found a higher incidence of low birth weight less than 10 percentile (53% versus 21%), in those who had a elevated S/D ratio (more than 90th percentile).2 Similar results have been found by Trudinger et al., and Seyam et al.15,16

**Meconium Stained Liquor**
The UA S/D Ratio is lower in normal liquor group than in the MSL group, which shows a higher umbilical vascular resistance in those foetuses who had intrapartum foetal distress. Our findings are in consonance with those of Ogunyemi, who found that those fetuses with elevated umbilical artery S/D ratio had higher incidence of meconium aspiration.17

**NICU admission and Low Apgar Score**
It was observed that S/D Ratio of the UA is higher in those foetuses that needed NICU admission than those who did not. Other studies have also found that those foetuses with elevated S/D ratio had higher incidence of NICU admission.6,18 S/D Ratio of UA is higher in those foetuses that had Apgar < 7 than those who had Apgar > 7. Various authors found that an elevated S/D ratio was significantly associated with a low Apgar at 5 minute.11,18,21

Kwon et al., studied umbilical and uterine artery doppler velocimetry in pregnancies with borderline amniotic fluid index and found that presence of abnormal doppler velocimetry measurement (umbilical artery S/D > 3) was related to increased risk of adverse perinatal outcome like 5 min Apgar score less than 7, NICU admission and perinatal death.18

**Middle Cerebral Artery –Birth Weight**
A decrease was observed in the PI of MCA with increase in birth weight, being lowest in less than 1.5 kg group and highest in 2 to 2.5 kg group. This is in consonance with studies by various authors.7

**CPR**
The CPR quantifies redistribution of cardiac output by dividing doppler indices from representative cerebral and fetoplacental vessels. The ratio shows a greater variation and appears to offer earlier detection of foetal adaptation to placental insufficiency than either the umbilical or middle cerebral artery. CPR or the MCA / UA resistance index < 1 is used to predict cases at high risk of perinatal morbidity and mortality.6,12,18 The ratio has been found to be a more sensitive marker for growth restriction (sensitivity 78%) than conventional foetal biometry and umbilical arterial S/D ratio.18

**CPR and NICU Admission**
CPR was less than one in those foetuses that needed NICU admission and more than one in those who did not need NICU admission. Piazze et al., studied PI of MCA and UA in 72 pregnant women with IUGR and using multiple logistic analysis found that UA/MCA PI ratio was the only doppler parameter predicting cardiacographic non reactivity and prolonged neonatal hospitalisation.19 Various other authors also reported that the MCA to UA resistance index ratio less than one is associated with prolonged NICU stay.12,19 Obido et al., also suggested that CPR less than 1.08 predicts adverse perinatal outcome like 5 minute Apgar score < 7 and perinatal death with sensitivity and specificity of 72% and 62% respectively.20

**CPR and Birth Weight**
In the present study CPR has been found to be lowest in extremely low birth weight group and rises as the birth weight increases. This is in consonance with the findings of Arias and Chan et al.6,13 In a study period of 2 years, Chan et al observed that foetuses who had a high prenatal umbilical-cerebral doppler ratio had significantly lower birth weight ratios than those with normal findings.13
Other doppler parameters have also been assessed in literature. This includes umbilical vein pulsation which has been reviewed by Borowsky et al. He studied CPR and PI in MCA and UA and also flow in the umbilical vein. He concluded that the presence of umbilical vein pulsation or deceleration of the brain sparing effect is closely related to increased perinatal mortality. Similar deceleration has also been found in the case of neonatal death in our study that showed a high PI of 1.56 in MCA with a low CPR of 0.592. Later studies in an effort to find answer to the conflicting studies evaluated a new parameter i.e. high Peak Systolic Velocity of MCA, which was found to be better than PI of MCA in predicting perinatal mortality. Further research is needed in this direction.

**CONCLUSION**

This study quantifies the impact of arterial doppler parameters on neonatal outcome in patients with foetal growth restriction. An area that needs attention is the modification of neonatal management based on antenatal testing information. The ability to predict increased risks for perinatal morbidity and mortality opens numerous vistas for neonatal management.

The UA Doppler waveforms in isolation are unsuitable as a test for foetal well being. In prenatal Doppler, documentation of altered brain perfusion marks an important step in foetal response to placental insufficiency. The CPR as an index of foetal well being was described over a decade ago. However, non-uniform doppler technique and variation in normative data have hindered the clinical utility of these Doppler parameters. Further studies in this direction will help us to address these concerns.

**About the Authors**

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**REFERENCES**

Current Management of Antenatal Hydronephrosis—An Update

Yap Te-Lu, MBBS, FRSC; Anette Sundfor Jacobsen, MB BCh, FRCS, M Med, FAMS

INTRODUCTION

Antenatal hydronephrosis (ANH) is a general term used to describe the dilatation of the fetal renal pelvis and/or its calyces. In pelviectasis, there is only dilatation of the renal pelvis; while in caliectasis, there is dilatation of the calyces. ANH is the most commonly diagnosed congenital urinary tract anomaly, which is detected by prenatal screening in 1–5% of all pregnancies.

In the early years of routine fetal ultrasound screening, almost all cases of ANH were subjected to invasive imaging studies postnatally, followed by a pre-emptive surgical approach. The management of ANH has since trended towards a more conservative approach over the past two decades. This shift is attributed to the better appreciation of the natural history of ANH and more accurate antenatal diagnosis.

In our current era, the approach to ANH should have the following goals: accurate antenatal identification of high-risk ANH; and minimal postnatal imaging for low-risk patients but aggressive and early surgical intervention for high-risk uropathies. Even though prenatal diagnosis allows for the planning of appropriate postnatal care, this benefit should be weighed against undue parental anxiety or even distress.

WHAT CONSTITUTES ANH?

Two widely accepted systems based on ultrasound images are used internationally for grading the severity of renal pelvis dilatation: the anteroposterior diameter (APD), a quantitative measurement of the dimension of the pelvis; and the Society of Fetal Urology (SFU) grading, which is a qualitative observation of the degree of pelvic and calyceal dilatation. The degree of renal pelvic dilatation, however, may be modified by the fetus gestational age, degree of fetal bladder distension, and maternal hydration status.

APD Measurement

The APD system measures the anteroposterior diameter in millimetres of the renal pelvis on the transverse plane at its point of exit from the kidney. It does not take into account all of the distribution (segmental or general), degree of calyceal distension or parenchymal thickness. However, this is the most widely adopted quantitative parameter in obstetric practice, especially outside North America.

As with most numerical threshold values for pathological diagnosis, the choice of the cut-off point involved a fine balance between sensitivity and specificity. Studies attempting to define the normal range of APD for a fetus have found that the maximum dimension of a normal renal pelvis at any gestational age is less than 5 mm in 92.7% of cases. Therefore, a level below 4 mm in the second trimester has been identified as the lower acceptable limit for a likely normal postnatal outcome. However, there is still controversy as to the threshold value for the third trimester to adopt for predicting postnatal pathology, be it 7 or 9 mm. A strict criterion of 7 mm on a 33-week gestation ultrasound will lead to a 100% detection of all hydronephrosis but also a high false-positive rate of 30–80%. On the other hand, Mallik and Watson illustrated that by increasing the APD cut-off for the third trimester to 10 mm, it will miss out on 25% of cases with pelviureteric junction obstruction (PUJO) and 50% with vesicoureteral reflux (VUR); conversely, only 23% with benign dilatation would be included.

The third-trimester APD has the highest positive predictive value in predicting postnatal uropathies. It is thus universally agreed upon...
that an APD greater than 15 mm in the third trimester would predict severe hydronephrosis and significant postnatal uropathies.

**SFU Grading of Pelvic Dilatation**

This 5-point grading system was first introduced by Fernbach et al\(^6\) in 1993 and has been widely adopted in North America. It takes into account the degree of calyceal dilatation and parenchymal thinning in classifying prenatal hydronephrosis. This system has been shown to have good intra-rater reliability but only modest inter-rater agreement.\(^7\) It has been proposed recently that this grading system be fine-tuned by further defining segmental versus diffuse cortical thinning.

**Secondary Sonographic Features**

In addition to the presence and severity of renal pelvic dilatation, antenatal sonogram should also assess the thickness and nature of the renal parenchyma, ie, the echogenicity, presence of renal cysts, and degree of corticomedullary differentiation. The best indicator of renal dysplasia and thus compromised function is hyperechoic renal parenchyma with presence of cortical cysts.\(^5,5\) It is pivotal to estimate the quantity of amniotic fluid and the development of the fetal lungs. A general assessment of the fetus to detect other congenital malformation and amniocentesis for chromosomal defects should be undertaken if deemed necessary. More refined assessments of the fetus’ renal function involve identifying the fetal urine biochemistry, eg, sodium, chloride, potassium and microglobulin.

**Predictive Value of APD for Postnatal Uropathies**

In general, infants with any degree of ANH are at greater risk of having a postnatal anomaly as compared with the normal population.\(^10\) Increasing degree of severity of ANH is clearly associated with a higher incidence of and more significant uropathies. According to a review and meta-analysis of 17 studies involving 1,308 subjects, the respective risks for mild, moderate and severe degrees of ANH for postnatal pathologies were 56.7–88%, 10.2–29.8%, and 1.5–13.4%, respectively.\(^11,12\) Overall, the risk is 36% for postnatal pathology of any degree of ANH detected in utero. However within each of the groups, there is a different distribution of the uropathies.

In the ‘mild’ group (APD 7–9 mm), only 11.9% of the ANH demonstrated a postnatal anomaly. For moderate ANH with APD between 9 to 15 mm in the third trimester, the incidence of PUJO was higher than that of VUR (17% vs 11%). A significant proportion of patients in this group have ureteral obstruction. In contrast, for the ‘severe’ group with APD greater than 15 mm, most of the pathology was attributed to PUJO (54.3%). In total, 88.3% in this group had significant postnatal anomalies.

Coplen et al\(^13\) in their studies of 257 neonates, found that a threshold limit of APD of 15 mm would differentiate obstruction from non-significant dilatation in 80% of fetuses with a sensitivity of 73% and specificity of 82%.

However, it has been shown that ANH detected in early pregnancy may stabilize or even resolve completely. In a systematic review of the literature, Sidhu et al\(^14\) documented a resolution rate of 72% for all grades of ANH. Ninety-eight percent of patients with SFU grades 1 and 2 of ANH showed stabilization, resolution or improvement of pelviectasis. But only 51% of SFU grades 3 and 4 eventually stabilized. Most investigators would therefore recommend repeat or serial ultrasounds to be performed again in the later part of pregnancy, as renal and ureteral biometrics are known to fluctuate. It has been shown by Thornburg et al\(^15\) that third-trimester ultrasound was a better predictor of surgically relevant hydronephrosis than second-trimester ultrasound.

It is equally important to be aware of an atypical group of patients with APD below the threshold value of 4 mm and 7 mm for the second and third trimesters, respectively, which would not merit any postnatal investigation. In a study by Chaviano et al,\(^16\) 13% of cases in their Virtual Pediatric Urology Registry of 1,128 patients were within this cut-off limit of which 20% eventually required extensive urological care postnatally. In another prospective cohort study of mild ANH with APD of 5–9.9 mm, 18% eventually demonstrated urological anomalies (mostly VUR) and 7.8% presented with urinary tract infection during a median follow-up period of 24 months.\(^17\)

**Other Ultrasound Parameters/Score Used for ANH**

Novel methods have been suggested in attempts to improve the categorization of severity of ANH. One of them is the hydronephrosis index: hydronephrosis index (percentage) = 100 x (total area of the kidney – area dilated pelvis) / (total area).\(^18\) Another attempt to overcome the effects of a distended fetal bladder for ANH is to divide the anteroposterior diameter of the renal pelvis by the bladder volume.\(^19\) Zhan et al\(^20\) devised a prenatal ultrasound score utilizing fetal APD, renal parenchyma thickness, and pelvicalyceal morphology. Values of 0 to 3 were assigned.
to each kidney studied. The total score ranges from 0 to 9, with the best pathological cut-off value of 6 differentiating between physiological fetal dilatation and pathological hydronephrosis.

Fetal Magnetic Resonance Imaging

Although ultrasound remains the modality of choice for imaging ANH, fetal magnetic resonance imaging is beginning to emerge as a valuable complementary tool for complex urological anomalies. It allows for exquisite demonstration of both normal and abnormal renal anatomy. Fetal magnetic resonance imaging is especially valuable in cases when the ultrasound findings are inconclusive. Its use, however, is still fairly limited.

AETIOLOGIES OF ANH

The possible postnatal diagnosis of ANH includes PUJO, transient hydronephrosis, VUR, non-refluxing megaureter, duplex kidneys with ureterocele or ectopic ureter, posterior urethral valve (PUV), urethral atresia/stenosis, and ureteral obstruction.

Pelviureteric Junction Obstruction

Pelviureteric junction obstruction is the commonest cause of pathological ANH (40–60%) with an incidence of 1 in 2,000 live births. It is three times more common in males and may be bilateral in 20–25% of cases. The proposed aetiology includes intramural fibrosis at the pelviureteric junction, abnormally high insertion of the ureter, extrinsic compression from crossing vessels, and adhesion. The classical ultrasound findings are calyceal and renal pelvis dilatation in the absence of a hydroureter.

In the pre-antenatal screening era, pyeloplasty was performed mainly for symptomatic kidneys. The concern was that unrelieved obstruction could potentially lead to near-total loss of kidney function. Thus, in the early antenatal screening period in the 1980s, almost all ANH cases that were diagnosed as ‘pelviureteric junction obstruction’ were subjected to early pre-emptive pyeloplasty based on the treatment philosophy, which was tailored for symptomatic ‘chronic’ PUJO. The natural history of antenatal ‘pelviureteric junction obstruction’ and the concept of ‘significant obstruction’ (ie, obstruction associated with compromised renal functions) soon began to surface in the 1990s. The landmark randomized controlled trial that illustrates the benign course of antenatal PUJO was published by Dhillon et al from the Great Ormond Street Hospital, London. Patients were randomized into two arms: 48 children who had pyeloplasty, and 52 who were managed conservatively. Of the 52 kidneys managed conservatively, 9 (17%) had deterioration of function during the observation period. However, 14 showed evidence of resolving obstruction while 29 out of 52 (56%) retained stable function despite radionuclide scans revealing persistent obstruction. Amongst the studies that support initial conservative management were those by Koff et al on 104 newborns with unilateral severe hydronephrosis who were managed conservatively. Only 23 required surgery for decreasing renal function, while 69% of the hydronephrosis resolved over an average period of 2.5 years with no deterioration of renal function.

The current surgical approach has tended towards an initial ‘watchful wait’ while surgery has been reserved for cases with a deteriorating trend of renal function or progressive renal dilatation. Randomized trials have so far indicated that only 19–25% of prenatally diagnosed PUJO eventually required surgical intervention.

Transient Hydronephrosis

The majority of the patients with ANH (41–88%) have a non-pathological dilatation of the kidney that either resolves spontaneously in the fetus or stabilizes with no further deterioration over time. Therefore, surgical intervention is not recommended for these patients. This transient pelvic dilatation, which is termed ‘transient hydronephrosis’, may be the result of:

1. Physiologically slow canalization of the ureter and maturation of the excretory system.
2. Transient ‘real’ impairment to the urinary out-flow giving rise to self-limiting prenatal dilatation. This has been postulated to result from a delayed maturation of the pelviureteric or vesicoureteric junctions.
4. Low-grade transient VUR that resolves spontaneously with no urinary tract infection episodes.

Even though ureteric canalization is achieved at the end of embryogenesis, maturation of the ureteric wall continues well beyond birth. In a study by Thomas et al to monitor long-term progress of mild pelvic dilatation in 29 children over a mean period of 4.2 years (range 1.5–7.8 years), 69% of the kidneys reverted to normal while the remaining 31% were diminished in size or were unchanged. Nevertheless, it remains exquisitely challenging to differentiate between transient hydronephrosis and pathological dilatation.
Transient hydronephrosis is the mild to moderate degree of pelvic dilatation in a normal-sized kidney which has no coexisting parenchymal compromise. There should also be no calyceal and ureteric dilatation or bladder abnormality. As a guide, almost all kidneys with an APD less than 6 mm in the second trimester or less than 8 mm in the third tend to be transient hydronephrotic. On the contrary, in kidneys with an APD of 12 mm in the third trimester or less than 8 mm in the third tend to be no calyceal and ureteric dilatation or bladder abnormality. There should also be no calyceal and ureteric dilatation or bladder abnormality. As a guide, almost all kidneys with an APD less than 6 mm in the second trimester or less than 8 mm in the third tend to be transient hydronephrotic. On the contrary, in kidneys with an APD of 12 mm in the third trimester, only 40% will eventually prove to be transient hydronephrotic.

Of note, one must be aware of the wide overlap of antenatal APD threshold values for transient hydronephrosis and pathological dilatation.

Vesicoureteral Reflux

Vesicoureteral reflux is the retrograde flow of bladder urine into the upper urinary tract owing to an incompetent vesicoureteric junction. This may result in infective, immunological, biochemical and/or urodynamic insults to the kidneys. Reflux nephropathy has been documented as the cause of end-stage renal failure in 21% of patients under the age of 19 years in 12 registries from Europe.

The American Urological Association (AUA) Pediatric Vesicoureteral Reflux Guidelines Panel in 2010 published a meta-analysis of 34 studies on 4,756 patients with prenatal hydronephrosis and VUR. They established an APD threshold criterion of 4 mm during the second trimester and 7 mm during the third trimester for the diagnosis of ANH at risk for VUR. The prevalence of VUR in patients with ANH in the above studies ranges from 7% to 35% with an average of 16.2%. However, micturating cystography (MCU) was not universally performed for all patients.

Regarding spontaneous resolution of reflux, patients with VUR diagnosed antenatally experienced a speedier resolution than those presented postnatally. In seven published series with 413 antenatally detected refluxing units, the short- to medium-term resolution rate for VUR grades 1–3 was 78% while that of grades 4 and 5 was 36%. These differ from the historical resolution nomograms development by the AUA for symptomatic cohorts. The deviation may be explained in part by the delayed maturation of the sphincter/bladder neck mechanism seen as high voiding pressures during early infancy.

On the other hand, antenatal diagnosis may have pre-selected a group of male infants with bilateral high-grade VUR associated with congenital renal dysplasia. This was revealed by Caione et al in a series of 50 patients with antenatally diagnosed bilateral high-grade VUR. After a follow-up period of a mean of 6.3 years (range 1–16 years), all the patients with chronic renal impairment were male. This was confirmed by Assael et al in a similar series of 108 patients of which 76 were male. It is this group of patients that mandate long-term follow-up by the nephrologist because of the high risk of developing chronic renal failure in puberty.

The AUA panel thus recommends that MCU be performed for all infants with high-grade postnatal hydronephrosis (SFU grades 3 and 4), hydrourerter or abnormal bladder, or those who develop urinary tract infection while on follow-up. The frequently cited reasons of opponents to the routine performance of MCU for mild ANH include low diagnostic rate, complication of MCU, radiation exposure, and cost ineffectiveness. Given the unproven value of identifying and treating VUR in infants with mild ANH (SFU grades 1 and 2), a cautious observational approach is one option. But parents must be cautious about the risk of urinary tract infection and the need to seek early treatment.

Non-refluxing Megaureter

Dilatation of the ureter that is not caused by reflux accounts for about 10% of ANH and has an incidence of 1 in 6,500 live births. The ‘obstruction’ may be due to a narrowed area or a localized segment of dysfunction of the distal ureter. The suspicion is first raised by the presence of antenatally detected unilateral hydronephrosis, communicating hydrourerter, and a normal urinary bladder.

The initial management of non-refluxing megaureter is observation, as it has an even higher resolution rate than PUJO of up to 72%. Shukla et al reported a series of 27 patients with 40 non-refluxing megaureters managed conservatively over a mean period of 6.8 years. Complete resolution was seen in 21 ureters (52.5%) with 19 (47.5%) showing improvement or stable findings. This was confirmed by McLellan et al on the follow-up of megaureters which showed that SFU grades 1, 2 and 3 hydronephrosis resolved over 13, 24 and 35 months, respectively. But for degree of dilatation greater than SFU grade 3 hydronephrosis, the resolution period may take up to 49 months on the average. The patient should, however, receive prophylactic antibiotics and regular ultrasound scans during this ‘watchful’ period.

Most series reported an operative rate of 10–20%. The predictive factors for surgery may include pelvic dilatation of SFU grades 3 and 4, differential renal function of less than
30%, and a ureteral diameter greater than 1.33 cm. We favour a single-stage ureteral re-implantation, likely with ureteral tapering.

**Duplex Kidneys With PUJO or Ureterocele/Ectopic Ureters**

Hydronephrosis can affect either the upper or lower moiety of the duplex kidney. Obstruction of the lower moiety is invariably at the level of the pelviureteric junction. The indication for surgical intervention in this case is similar to that of PUJO in a single kidney. The exception is the technical details of the surgical correction. For duplex kidneys with low ureteral bifurcation, the standard dismembered pyeloplasty is appropriate. However, for high ureteral bifurcation with a short segment of lower moiety ureter distal to the PUJO, an end-to-side anastomosis between the lower moiety pelvis and the upper moiety ureter is favoured.

Obstruction of the upper moiety of duplex systems resulting in dilatation of the corresponding pelvicalyceal system is caused by either an ureterocele or an ectopic ureter. The anomaly is identified on antenatal screening with an incidence of 5–7%. The diagnosis can easily be confirmed by the presence of a massively dilated ureter, a duplex kidney, and visualization of a cystic structure within the urinary bladder on ultrasound. Further postnatal imaging should include micturating cystogram, dynamic radionuclide scan, and even magnetic resonance urography.

The condition may emerge as a neonatal emergency if the ureterocele becomes prolapsed and causes bladder outlet obstruction. A simple cystoscopic puncture of the ureterocele will suffice. Main surgical decision making will depend on the function of the upper moiety and the presence or absence of a refluxing lower moiety ureter. If the upper moiety is of good function, preservation is an option by either cystoscopic incision of the ureterocele or resection of the ureterocele followed by re-implantation of the ureters. Similarly for the ectopic ureter, common sheath re-implantation of ipsilateral ureters is the operation of choice for preservation of the upper moiety. However, if the upper moiety demonstrates minimal function with a massively dilated ureter, laparoscopic upper hemi-nephroureterectomy is proposed.

**PUV and Urethral Atresia**

Posterior urethral valve is the most common cause of lower urinary tract obstruction in neonates, with an incidence of 1 in 5,000–8,000 live births. The fetus is invariably male. Typical ultrasound findings are that of bilateral hydronephrosis, hydroureters, and distended and thick walled urinary bladder with dilatation of the posterior urethra. In addition, there is frequently associated renal dysplasia with occasional presence of perinephric urinoma or fetal ascites. The high perinatal mortality rate is attributed to the severe oligohydramnios and the resultant pulmonary hypoplasia. In the latest annual report of the UK renal registry, obstructive uropathy accounted for 16% of children with end-stage renal failure of whom 89% were male with PUV. However, data from the literature is inconclusive on the benefit of antenatal drainage. It may increase perinatal survival with improved lung development but has not been shown to optimize renal prognosis by limiting the degree of congenital renal dysplasia.

Nevertheless, the classic scenario of neonates with PUV presenting with life-threatening urosepsis is extremely rare nowadays, as about 80% of the cases are detected prenatally. MCU should be performed urgently at birth to confirm the diagnosis, thus enabling early ablation of the PUJ or vesicostomy for decompression of the upper tract. It is essential that metabolic abnormalities be corrected as soon as possible and urosepsis should be prevented.

Of those who survive the neonatal period, 17–30% will eventually develop end-stage renal impairment necessitating dialysis or transplant. The presence of bilateral VUR with recurrent urinary tract infections are poor prognostic indicators.

**Multicystic Dysplastic Kidney**

Although strictly not part of the aetiology of ANH, multicystic dysplastic kidney (MCDK) has been mistaken for gross hydronephrosis. The diagnostic features on ultrasound that must be verified include multiple non-communicating randomly distributed cysts of variable sizes, lack of identifiable renal parenchyma, and a non-dilated ureter. It is well documented that MCDK has an excellent potential for spontaneous involution. Narchi reviewed 26 published series of MCDK involving 1,115 children managed conservatively; there were no cases of malignant change and only six reported cases of hypertension. Ismaili et al has shown in their study that two successive normal postnatal ultrasound scans may suffice to rule out clinically significant uropathies of the contralateral kidney.

**POSTNATAL EVALUATION OF ANH**

The postnatal evaluation of ANH should follow a systematic and comprehensive imaging
protocol that examines both the upper and lower urinary tract. Nonetheless, one should attempt to avoid unnecessary investigation during physiological and low-risk conditions.

Ultrasound
Ultrasound examination is radiation-free, safe, quick, cheap, and repeatable. It makes an excellent screening tool for neonates with ANH and for the planning of subsequent postnatal management. In the normal neonate, there is relative dehydration with decreased urine output for the first 24–48 hours of life. Therefore, too early a postnatal ultrasound may miss a borderline hydronephrosis or underestimate a severe one. The initial ultrasound must assess the degree of dilatation of the pelvicalyceal system, any dilatation of the ureters, estimated size of the bladder and thickness of its wall, as well as the status of the renal parenchyma (thinning, dysplasia, cysts, impaired perfusion). One should be vigilant of any renal duplication with possible coexisting ureterocele. Ultrasound assessment of the posterior urethra should be the routine if there are bilateral secondary obstructive changes.

Additional information can be obtained by combining ultrasound with contrast-enhanced voiding urosonography to detect VUR. Ultrasound contrast media utilizing microbubbles have gained approval in several countries. The latest advancement in ultrasound technology includes duplex Doppler sonography, amplitude-coded colour Doppler sonography, three-dimensional ultrasound, and three-dimensional ultrasound-based virtual cystoscopy.

Micturating Cystography
Micturating cystography is an invasive procedure involving per-urethral catheterization and the instillation of radiopaque contrast media into the urinary bladder. The examination delivers a substantial quantity of radiation to the abdomen and pelvis, particularly in patients with complex malformations. Various modifications and improvements to its technique have arisen following new insights into the importance of a physiological rate of bladder filling, pitfalls with low-grade VUR, and the need for post-void assessment.

The overall incidence of VUR in the neonates with ANH varies between 8% and 38% in different studies. As neither the degree of ANH nor the gender of the child can help to predict the presence of VUR in children with ANH, there is currently no clear evidence to support or eliminate postnatal imaging for VUR. It is widely accepted that MCU should be offered to infants with postnatal pelvis dilatation of more than 7 mm in any one of two consecutive postnatal ultrasound examinations performed 1 month apart.37

Renal Scintigraphy: Dynamic Renal Scans
Dynamic or excretory renal scans are used to distinguish upper urinary tract obstruction from a dilated but non-obstructed collecting system. Either isotopes, mercaptoacetyltriglycine (MAG-3) or diethylenetriaminepentaacetic acid, may be used with or without a diuretic. MAG-3 is principally cleared from the kidney by tubular secretion. It generates excellent images of both the parenchyma and the collecting system, thus enabling quantification of their excretory function. MAG-3 is the preferred agent for diuretic scans.

Guidelines have been formulated by the European Association of Nuclear Medicine49 to standardize the interpretation of the drainage curve. The normal differential function of each kidney is in the range of 45–55%. Interpretation of the kidney’s drainage status, however, is not always straightforward and equivocal results are common. This is because multiple factors, both physiological and pathological, may influence the kidney’s drainage ability. There may also be ‘over-estimation’ of the function of massive hydronephrotic kidney leading to supra-normal readings.50

Most surgeons use drainage pattern as well as differential renal function in conjunction with serial ultrasound imaging trend to optimize the prediction for surgical intervention.51

Static Dimercaptosuccinic Acid Renal Scan
Technetium Tc 99m dimercaptosuccinic acid (DMSA) renal scan is the standard modality used for evaluation of the renal parenchyma. The radioisotopes bind to the proximal renal tubules after intravenous injection. Its radioactivity pattern is then captured and ‘translated’ into static images of the kidneys 2–4 hours later. DMSA is a highly sensitive and accurate tool for detecting cortical scarring and functional renal tissue, and estimating the differential function of each kidney.

Magnetic Resonance Urography
Magnetic resonance urography (MRU) provides high-resolution images of the whole urinary tract and its surrounding structures with no exposure to radiation. Its distinct advantages include its three-dimensional reconstructive capabilities and quantification of various renal functional indexes such as calyceal and renal transit times, glomerular filtration rate and differential renal functions. Nevertheless,
sophisticated computer software is essential for these advanced applications.

MRU has been shown to be superior to radionuclide studies in distinguishing between pyelonephritis and scarring. It is especially informative for duplex system with minimal functioning upper moiety. MRU, therefore, has the potential to replace ultrasound and renal radionuclide scintigraphy in the investigation of ANH. The major impediment with MRU is the excessively long image acquisition time and its extreme sensitivity to motion artifact. This translates to the necessity of general anaesthesia for neonates, infants and even younger children.

POSTNATAL IMAGING ALGORITHMS FOR ANH

Controversy still exists in the literature regarding the extent of postnatal imaging for mild ANH (SFU grades 1 and 2). We recommend the European Society of Paediatric Radiology imaging recommendations in paediatric uroradiology: two postnatal ultrasounds 4 weeks apart as screening. It has been shown by the Brussels Free University Perinatal Nephrology Study Group that significant nephropathies were diagnosed in 39% of their 213 infants with mild to moderate pyelectasis when followed up for 2 years. Therefore, it is important to follow up even the mild and moderate ANH postnatally with at least two ultrasound examinations. By repeating the ultrasound, the predictability for significant uropathies has been shown to improve to a sensitivity of 96%, specificity of 76%, positive predictive value of 72%, and a negative predictive value of 97%.

However, for infants with moderate to severe hydrenephrosis, a more intense and sophisticated protocol must be employed, ie, urgent MCU followed by early diuretic renal scan.

Conversely, dilatation detected in the second trimester but resolved by the third trimester may still have a 12% risk of significant anomalies. Therefore, parents should be advised on the possibility of late presentation of PUJO.

Prophylactic use of antibiotics is not universally agreed upon. Prenatal screening has been responsible for a drastic decrease in urinary tract infection, but occasional infection still occurs.

To ensure that antenatal detection and postnatal follow-up go hand in hand, all efforts must be made to educate parents on the risk of renal damage from infection and neglect. An antenatal consultation with a paediatric urologist or surgeon may be the key to better compliance.

CONCLUSION

Over the past two decades, the natural history of ANH has become better understood and appreciated. Prenatal diagnosis has undoubtedly improved the survival outcome and reduced the morbidities of most congenital urological anomalies.

However, ‘perfect’ and cost-effective management strategy guidelines derived from evidence-based research are not yet available. Understandably, randomized trials in the realm of maternal–fetal medicine and paediatrics are at best difficult if not impossible to develop and execute. Therefore, the next best option may be the setting up of a collaborative registry on ANH between regional centres and even countries.

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A complete list of references can be obtained upon request to the editor.