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Khartoum Medical Journal Objectives

1. Provide a forum for scientific and clinical medicine publications.
2. Serve the medical community in Sudan and the region in the field of continuing medical education.
3. Offer opportunities for the publication of service-oriented research and disseminate information aimed at the promotion of health services.
4. Encourage the development of medical and allied sciences research.
5. Provide opportunities for development of expertise in medical and allied sciences education.
6. Act as a platform for the expression of professional and scientific opinion and exchange of information.
7. Provide a forum for the exchange of ideas and experiences in the field of education and training in the medical and health professions.
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Obstetric nephrology: The effects of pregnancy on the kidney and the kidney on pregnancy
Ibrahim H Fahal
Department of Renal Medicine and Transplantation. The Royal London Hospital

Introduction
Normal pregnancy imposes physiological and occasionally pathological changes on the kidney and pregnancy in women with chronic kidney disease (CKD). This condition is associated with risks of accelerated decline in renal function in the mother and adverse outcomes for the infant. The management of the kidney in the pregnant woman presents a major challenge. The clinician has two patients; the mother and the foetus and two situations; the patient with CKD who becomes pregnant and the pregnant woman who develops kidney disease.

Hence, Obstetric nephrology is a growing subspecialty within nephrology. This article presents an overview of the common renal problems encountered during pregnancy and the effect of pregnancy on pre-existing renal disorders.

Pregnancy and the kidney
Pregnancy imposes physiological and pathological changes on the kidney in various ways.

Pregnancy and renal haemodynamics
Normal pregnancy is associated with marked haemodynamic alterations within the maternal circulation. Circulating blood volume and red blood cell mass increases by 50%, systemic vascular resistance and arterial blood pressure falls and cardiac output increases by up to 30%. These cardiovascular adaptations have profound effects on renal function leading to increase renal blood flow by as much as 85% in second trimester secondary to increased cardiac output, increased renal vasodilatation of both afferent and efferent arterioles. Glomerular filtration rate (GFR) rises immediately after conception, reaching about 30% above baseline and resulting in significant hyperfiltration in second trimester; GFR then falls by about 20% in last trimester, returning to prepurpartum levels within 3 months of delivery. Normal plasma creatinine falls to 0.5 mg/dL (51 μmol/L) and any value above 0.85 mg/dL (75 μmol/L) should be considered abnormal; there is also a respective fall in blood urea nitrogen.

Renal tubular changes allow for the accumulation of nutrients and electrolytes necessary for foetal growth such that wasting of proteins, glucose, and amino acids in urine is limited in pregnancy and total body stores of electrolytes increase throughout gestation.

Increased GFR, changes in glomerular haemodynamics and possibly alterations in renal tubular function lead to an increase in urine protein excretion in pregnancy from an upper limit of 150 mg/24 hr to 260 mg/24 hr. Renal size increases by approximately 1 cm in bipolar length during normal pregnancy. Smooth muscle relaxation and compression of the ureters by the gravid uterus commonly lead to pelvicalyceal dilatation, more prominently on the right than the left.

Hypertensive disorders of pregnancy (HDP)
Hypertensive disorders of pregnancy (HDP) are a leading cause of maternal mortality worldwide, complicating 5–10% of all pregnancies (1,2) and the incidence of hypertension in pregnancy continues to increase (3).

Blood pressure falls in the first two trimesters and gradually returns to baseline as the pregnancy approaches term. This is due to the peripheral vasodilatation and resistance to angiotensin II secondary to high prostacyclin and prolactin levels. Nitric oxide synthesis increases during normal pregnancy and may contribute to systemic and renal vasodilation and fall in BP mediated via relaxin, produced by placenta and corpus luteum (4).

Hypertension in pregnancy is defined as a persistent systolic BP greater than 140 mmHg or diastolic BP 90 mmHg. It has a bimodal frequency with young primiparous (3 to 8 times more susceptible) and older multiparous women mostly affected. Hypertension is considered severe when systolic blood pressure is ≥160 mmHg and/or diastolic blood pressure is ≥110.
mmHg, and mild when systolic blood pressure is $\geq 140$ mmHg and/or diastolic blood pressure is $\geq 90$ mmHg. There is no established definition for moderate hypertension in pregnancy.

There are four major hypertensive disorders related to pregnancy: gestational hypertension, preeclampsia and superimposed preeclampsia and chronic hypertension$^{5,6}$

The aims of treating hypertension in pregnancy are to reduce the risk of maternal cardiovascular or cerebrovascular events while not causing underperfusion of the placenta. There is no consensus on the optimal level of blood pressure control but some evidence suggests that being too aggressive may lead to a reduction in foetal weight$^{7,8}$.

**Gestational hypertension**

Gestational hypertension occurs in about 6 percent of pregnancies$^{9}$. However, some patients will develop proteinuria and be considered preeclamptic, while others will be diagnosed with preexisting chronic hypertension because of persistent blood pressure elevation postpartum.

The main objectives in the initial evaluation of pregnant women with newly developed hypertension are to distinguish gestational hypertension from preeclampsia, which has a different course and prognosis, and to determine whether hypertension is mild or severe, which affects management and outcome$^{10,11}$.

Gestational hypertension tends to recur with subsequent pregnancies$^{12,13}$ and is associated with development of hypertension later in life, and possibly associated with development of diseases related to hypertension$^{14-17}$.

**Preeclampsia and superimposed preeclampsia**

Preeclampsia is a multi-system disorder with renal, other system involvement and characterized by new-onset hypertension, proteinuria, and oedema, usually developing after 20 weeks of gestation$^{18}$. Superimposed preeclampsia is defined as chronic hypertension in the setting of new-onset worsening blood pressures, proteinuria ($>300$ mg of protein in 24 hours), thrombocytopenia, or any other systemic features of the preeclampsia syndrome$^{10}$. When seizures develop, it is known as eclampsia. The presence of a placenta, with or without a fetus (hydatidiform mole), is necessary for its development. Consequently, definitive treatment is by delivery of the placenta.

**Renal injury of preeclampsia**

Chronic kidney disease (CKD) and preeclampsia occur in 3–5% of pregnancies. They often share hypertension and proteinuria and a differential diagnosis may be impossible. Renal involvement in preeclampsia presents as proteinuria ($>300$ mg/24h or spot urinary protein: creatinine ratio of 30 mg/mmol), elevated plasma creatinine $>1.2$ mg/dl ($>90$ μmol/L) or oliguria. The characteristic lesion is glomerular endotheliosis which represents a specific variant of thrombotic microangiopathy that is characterized by glomerular endothelial swelling with loss of endothelial fenestrae and occlusion of the capillary lumens$^{19}$. Unlike thrombotic microangiopathy, associated thrombosis is unusual. Recent evidence suggests that this unusual glomerular lesion is mediated by a soluble vascular endothelial growth factor receptor that deprives glomerular endothelial cells of the vascular endothelial growth factor that they require, leading to cellular injury and disruption of the filtration apparatus with subsequent proteinuria$^{20}$.

**Consequences of preeclampsia**

Although glomerular endotheliosis in general is believed to resolve completely after delivery, recent evidence suggests that preeclampsia may leave a permanent renal damage. Several investigators have suggested that preeclampsia have a four to five times increased risk of later CKD and microalbuminuria$^{21-24}$ for several years after pregnancy. The increased risk of CKD was strongest during the first 5 years after giving birth, but remained significant also after this period and renal biopsy studies identified different diagnoses$^{21}$. In addition, women who previously had preeclampsia had a four to five times increased risk of later end-stage renal disease, independent of primary renal disease$^{25}$.

**HELLP syndrome**

HELLP syndrome refers to hemolysis with a microangiopathic blood smear, elevated liver enzymes, and a low platelet count$^{26}$. HELLP
develops in approximately 1 of 1000 pregnancies overall and 10 to 20 percent of pregnancies with severe preeclampsia/eclampsia. The majority of cases are diagnosed between 28 and 36 weeks of gestation.

The most common clinical presentation is abdominal pain and tenderness in the midepigastrium, right upper quadrant, or below the sternum \(^{(27)}\). Many patients also have nausea, vomiting, and malaise, which may be mistaken for a nonspecific viral illness or viral hepatitis \(^{(28)}\). Hypertension and proteinuria are present in approximately 85 percent of cases, but may be absent in women with otherwise severe HELLP syndrome \(^{(29)}\). The diagnosis of HELLP syndrome is based upon the presence of the laboratory abnormalities comprising its name in women with a diagnosis of preeclampsia.

The outcome for mothers with HELLP syndrome is generally good, but serious complications such as abruptio placentae, acute renal failure, pulmonary edema, subcapsular liver hematoma, and retinal detachment may occur \(^{(27)}\). The risk of recurrence in future pregnancies appears to be increased.

Management of pregnancy with pre-eclampsia

The major indication for antihypertensive therapy in preeclampsia is prevention of maternal stroke and other complications of severe hypertension. Lowering blood pressure does not affect the course of preeclampsia because the primary pathogenetic process is an abnormality of the placental vasculature that results in placental underperfusion, which, in turn, leads to release of factors that cause widespread maternal endothelial dysfunction with multiorgan dysfunction.

Chronic hypertension

Chronic hypertension is defined as hypertension (>140 mmHg or diastolic blood pressure >90 mmHg) that is diagnosed before pregnancy or before 20 weeks of gestation. Hypertension that is first diagnosed after 20 weeks’ gestation and persists for greater than 12 weeks postpartum is also considered chronic hypertension \(^{(10)}\).

In pregnant women with uncomplicated chronic hypertension aim to keep blood pressure lower than 150/100 mmHg. There is no evidence that lowering diastolic blood pressure below 80 mmHg in women with uncomplicated chronic hypertension offers additional benefits and therefore treatment is not offered. Offer pregnant women with target-organ damage secondary to chronic hypertension (for example, kidney disease) treatment with the aim of keeping blood pressure lower than 140/90 mmHg.

Medical management of severe hypertension in a critical care setting

Treat women with severe hypertension during pregnancy or after birth immediately with one of the following; labetalol (oral or intravenous), hydralazine (intravenous) or nifedipine (oral) and continue to monitor their response to treatment to ensure that their blood pressure falls, identify adverse effects for both the woman and the fetus and modify treatment according to response. Consider using up to 500 ml crystalloid fluid before or at the same time as the first dose of intravenous hydralazine in the antenatal period. In women with severe hypertension, aim to keep systolic blood pressure below 150 mmHg and diastolic blood pressure between 80 and 100 mmHg.

Breastfeeding

In women who still need antihypertensive treatment in the postnatal period, prescribe one of the drugs that are likely to be safe if the woman is breastfeeding or expressing milk.

Recurrence risks and consequences of Hypertensive disorders of pregnancy (HDP)

Women who had gestational hypertension have the risk of developing:

- Gestational hypertension in a future pregnancy ranges from about 1 in 6 (16%) pregnancies to about 1 in 2 (47%) pregnancies.
- Preeclampsia in a future pregnancy ranges from 1 in 50 (2%) to about 1 in 14 (7%) pregnancies.

Women who had preeclampsia have the risk of developing:

- Gestational hypertension in a future pregnancy ranges from about 1 in 8 (13%) pregnancies to about 1 in 2 (53%) pregnancies.
- Preeclampsia in a future pregnancy is up to about 1 in 6 (16%) pregnancies.
• Preeclampsia in a future pregnancy is about 1 in 4 (25%) pregnancies if their preeclampsia was complicated by severe preeclampsia, HELLP syndrome or eclampsia, which led to birth before 34 weeks, and about 1 in 2 (55%) pregnancies if it led to birth before 28 weeks.

Long-term risk of cardiovascular disease
• Women who have had gestational hypertension or preeclampsia have an increased risk of developing hypertension and its complications in later life.

Long-term risk of end-stage kidney disease
• Women with a history of preeclampsia who have no proteinuria and no hypertension at the postnatal review (6–8 weeks after the birth) and although the relative risk of end-stage kidney disease is increased the absolute risk is low and no further follow-up is necessary.

• Women who previously had preeclampsia with hypertension and proteinuria had a four to five times increased risk of later end-stage renal disease, independent of primary renal disease (25).

Pregnancy induced renal disease
The aetiology of pregnancy induced acute kidney injury-AKI (previously known as acute renal failure) is varied and depends on the stage of pregnancy. The most common cause of pregnancy induced AKI is acute tubular necrosis associated with acute volume depletion. Pregnant patients appear to be particularly at risk from the devastasting complication of cortical necrosis, which results in irreversible renal failure. Hypertensive complications of pregnancy (preeclampsia/eclampsia or HELLP) are one of the leading causes of AKI in pregnancy worldwide (30). Thrombotic microangiopathy is another peculiar and devastating cause of AKI in pregnancy. Less commonly, patients present early postpartum with haemolytic–uraemic syndrome (HUS).

The later renal impairment occurs, the more likely it is to reflect pregnancy-induced renal disease. Preeclampsia and HELLP syndrome usually occur antepartum (although renal function may decline postpartum), whereas HUS classically occurs unexpectedly within days to weeks postpartum. Preeclampsia and acute fatty liver of pregnancy (AFLP) are more common in nulliparous women. HELLP syndrome is more common in multiparous women (31), the group most likely to develop acute kidney injury (13.5%). Acute renal dysfunction associated with preeclampsia or HELLP syndrome has an excellent prognosis. However, a significant proportion of patients with pre-existing renal disease or hypertension suffer irreversible decline or even loss of renal function; HUS generally has a much worse prognosis.

Others causes of AKI/renal impairment in pregnancy are obstructive uropathy and renal stones. Obstructive uropathy presents with moderate or severe dilatation of the collecting system and oliguria or anuria. The causes of this condition include a gravid uterus, polyhydramnios, kidney stones, and enlarged uterine fibroids. Obstructive uropathy usually resolves with delivery, although ureteral stenting may be required preterm.

Renal stones in pregnancy are caused by increased urinary calcium excretion in pregnancy due to increased intake and increased gastrointestinal absorption (32). Its presentation is the same as it is in the non-pregnant women, and there is an increased risk of urinary tract infection.

The kidney and pregnancy
Pregnancy in the setting of chronic kidney disease (CKD)
CKD is rare in pregnant patients, affecting 0.15% of pregnancies and most affected patients have early stages of CKD (estimated eGFR >45 ml/minute). The normal mean serum creatinine for a pregnant woman is 0.5mg/dl (51μmol/l) vs 0.82mg/dl (73μmol/l) in non-pregnant women and a creatinine of greater than 0.85mg/dl (75 μmol/l) after 6 weeks’ gestation should raise the suspicion of renal impairment. Proteinuria at the first ante-natal clinic visit or early in pregnancy should also raise the suspicion of renal disease. The presence of haematuria and proteinuria almost always suggests the presence of glomerular disease.

The degree of renal impairment and most importantly hypertension are the main influences on the course of a pregnancy and evidence suggests that hypertension
is the most important prognostic factor. Data suggests that foetal and renal prognoses are excellent in women with a serum creatinine level less than 1.4mg/dl (120 μmol/l) and no hypertension (33).

Obstetric and renal outlook are poorer in women with moderate renal impairment (creatinine over 1.41mg/dl (125 μmol/l) but less than 2.8mg/dl (250 μmol/l), with or without hypertension, and severe renal impairment (creatinine > 2.8mg/dl) is associated with a poor prognosis for both mother and fetus. Patients with renal disease that is likely to progress should be advised to become pregnant early in the course of their disease.

**Pregnancy and dialysis**

Pregnancy in dialysis patients is usually unexpected and therefore diagnosed late, and is associated with major problems for mother and baby. It needs intense monitoring and management.

**Pregnancy after Kidney Transplantation**

Fertility rates increase dramatically after transplantation in women with end-stage kidney disease and it is usual to advise transplant patients to postpone pregnancy for at least 1 year until graft function is stable and immunosuppression is at a relatively low level (36). Normal vaginal delivery is not contraindicated following renal transplantation but it is important to ascertain the position of the renal pelvic allograft and the ureter to plan delivery. A renal ultrasound is helpful to aid in precise location. This information should be placed in the prenatal record and if Caesarean section is indicated then a lower segment approach may be difficult due to the course of the transplanted ureter. Prophylactic antibiotics and careful wound closure are warranted to avoid complications in these immunocompromised patients.

For mothers with baseline creatinine less than 1.41mg/dl (125 μmol/l), successful pregnancy occurs in 97% of cases reaching the second trimester. However, the incidence of preterm delivery, intrauterine growth restriction and pre-eclampsia is greater than the general population and 30% of pregnancies may be affected.

Most evidence suggests that pregnancy after transplantation does not increase risk for loss of graft function (37), so long as the serum creatinine is less than <1.5 mg/dl (132 umol/litre). However the likelihood of accelerated maternal renal decline is high with significant renal dysfunction at conception. In one study, all transplant patients with creatinine greater than 2.26 mg/dl (200 umol/litre) at conception progressed to dialysis within 2 years.

Neonatal outcomes in pregnancies among renal transplantation patients are generally good. Most adverse neonatal outcomes are related to a higher rate of preterm birth (50 to 54%), small for gestational age (33 to 45%), and neonatal mortality (1 to 3%) as compared with the general population (12.3, 5, and 0.68%, respectively) (38, 39). The highest risk for preterm birth and small for gestational age are seen in the setting of maternal hypertension and impaired baseline renal graft function (creatinine >1.5 mg/dl) (38). Long-term developmental outcomes of surviving infants seem to be good (40).

Immunosuppressive medications need to be adjusted before conception or immediately on discovery. Calcineurin inhibitors (ciclosporin, tacrolimus), steroids, and azathioprine are the mainstays of safe immunosuppressive therapy in pregnant transplant recipients. Although there is many decades’ experience of use of these agents during pregnancy, women should be informed of the recognized patterns of reported side effects. At high doses (>20 mg/day) prednisolone can lead to foetal adrenal insufficiency and risk of maternal infection. Maintenance doses of less than 10 mg/d appear safe and well-tolerated in pregnancy. Ciclosporin and tacrolimus may exacerbate hypertension and limit renal adaptation to pregnancy. Foetal growth restriction may be associated with these agents. Azathioprine is teratogenic in high doses in animal studies. In humans it has been used without obvious teratogenicity but it may be associated with foetal growth restriction.

Trough serum levels of the calcineurin inhibitors tacrolimus or ciclosporin should be measured at every visit. Altered pharmacodynamics during pregnancy necessitates careful titration of doses of these drugs to maintain adequate levels whilst avoiding toxicity. A dose increase of up to 4-fold may be required and close monitoring in the puerperium is as important as during pregnancy with the need for dose reduction.

Mycophenolate mofetil (cellcept) and other
immunosuppressive medications are contraindicated in pregnancy.

**Conclusions**

Obstetric nephrology is a growing subspecialty within nephrology and highlights the importance of close and evidence based nephrology management and follow up during pregnancy to ensure a safe and viable pregnancy.

Ideally, an Obstetric Medicine/nephrology clinic should be set up for women with kidney conditions who are planning a pregnancy or expecting a baby which should combine the expertise of a consultant obstetrician who specialises in maternal medicine, a consultant nephrologist who specialises in kidney disease and pregnancy and senior midwives.

**Reference**


29. Sirbai BM. Diagnosis, controversies, and management of the syndrome of hemolysis, elevated liver enzymes, and low platelet count.


Introduction

The adolescence period covers the age of 10-19 years. This is a period of transition from childhood to adulthood\(^1\). Adolescence is a distinct and important biological and social stage of development. Pregnancy in a girl aged between 10-19 years is referred to as adolescent or teenage pregnancy. Around 16 million births (11% of all births) each year occur in teenage women, and almost 95% of these births are in developing countries.\(^1\) The incidence of teenage pregnancy varies worldwide and is high in Sub-Saharan Africa, some countries in South Asia and Latin America and Middle East. Half of all adolescent births occur in just seven countries: Bangladesh, Brazil, the Democratic Republic of Congo, Ethiopia, Nigeria, India and the United States. The five rich countries with the lowest teenage birth rates are Korea, Japan, Switzerland, the Netherlands and Sweden, all with teen birth rates of fewer than 7 per 1000.\(^2\) In Sudan, the birth rate is 52 per 1000 females aged 15-45 years. Thirteen percent of which were adolescent mothers aged <20 years.\(^6\)

There is great controversy regarding pregnancy performance of teenage mothers and studies have suggested that they were at higher risk of morbidity and mortality.\(^9\) Conditions associating adolescent childbearing and maternal health problems include obesity, anemia, malaria, sexually transmitted infections (STIs), mental illness, unsafe abortion complications, hypertensive disorders and obstetric fistula. Studies reported 50% higher rates of newborn death in adolescent mothers compared to mothers in their 20s. Other foetal complications include low-birth weight, birth asphyxia, prematurity and neonatal deaths. There was no significant difference in mode of delivery. Teenage pregnancy is associated with poverty, illiteracy, poor antenatal care attendance, loss of one or both parents and low contraceptive use. Rising levels of education, more career choice for women, more effective contraception, and changing preferences, have increased the average age at first birth in all developed countries. Studies showed that teenage mothers had higher proportion (65.7%) of normal vaginal delivery compared to older mothers (61.4%). About 34% of teenage mothers had instrumental delivery (forceps and caesarean) compared to 39% of the adult mothers. However,
the association between age of mother and mode of delivery was not significant (p>0.05). Stillbirth rate was significantly higher in teenage deliveries (5.1%) compared to 0.9% in the comparison group. Teenage pregnancy was significantly associated with low birth weight (<2.5 kg). The mean birth weight was 2.59 kg in the teenage group and 2.72 kg in the control group and the difference was highly significant. Study was conducted in 2009 at Khartoum Teaching Hospital compared maternal and perinatal outcome in teenage pregnancies found statistically significant difference between teenage primiparous and those aged 20-24 years; in level of education, antenatal care, anemia, low birth weight and mode of delivery.

The main objective of the study is to assess teenage pregnancy outcomes and compare these outcomes with those of pregnant women 20-29 years old. More specifically, the study aims to estimate foetal outcomes (Apgar score, birth weight, admission to Neonatal Intensive Care Unit (NICU) and stillbirth) and maternal outcome (Pregnancy induced hypertension, anaemia, antepartum haemorrhage, duration of labour, mode of delivery, postpartum haemorrhage and maternal mortality).

Patients and methods
Study setting and design
This is a prospective cohort study conducted at Omdurman Maternity Hospital, during June to September 2010. Omdurman Maternity Hospital had five units with two to four consultants in each unit. The hospital has two antenatal wards, four labour rooms, and two postnatal wards. There are about 25,000 deliveries per year in the hospital.

Teenage pregnancy is defined as pregnancy occurring during the maternal ages of 10-19 years at delivery while primigravida adult mothers aged 20-29 years forms the comparison group.

Data collection and analysis
Considering low birth weight as an important outcome of teenage pregnancy a pilot study conducted in the same hospital found 30.0% of low birth weight babies were born to teenagers while 14.8% of low birth weight babies were born to adult mothers aged 20-29 years. Using low birth weight as the primary outcome measure, G-Power analysis set for differences between two independent proportions was used to calculate sample size for the two groups. Power was set at 0.8, alpha level was set at 0.05 giving a sample size of 118 for each of the teenage and adult women groups. A total of 236 mothers comprised the study subjects.

An interview was conducted with women who attended to the labour room in Omdurman Maternity Hospital, during the period of the study and a structured clinical questionnaire was filled for women who met the inclusion criteria. The questionnaire comprised detailed medical history, examination findings at admission and socio-demographic characteristics. Both teenage and adult women were followed up to labour without interfering with hospital protocols. Consent was taken from each participant and confidentiality was kept. Data was analyzed using SPSS package comparing proportions of the two groups and using chi-square or Fisher exact tests to test for differences between proportions.

Results
Background characteristics
Background characteristics are summarized in Table 1. Significantly, more teenage mothers (29.6%) lived outside Khartoum State than adult mothers (17.8%) (P=0.032). Lower level of education (P=0.044) and lower socio-economic level (P<0.001) were significantly associated with teenage pregnancy. A significantly higher percentage of teenage mothers (34.7%) received no antenatal check-ups compared to adults (19.5%) while a lower percentage of teenage mothers (51.7%) received 5-7 visits compared to adult women (68.6%) (P=0.018).
Foetal outcomes are presented in Table 2. Teenage mothers (17.8%) had significantly higher proportion of lower Apgar score (<5) compared to adult mothers (6.0%) (P=0.005). Foetal birth weights tended to be lower among teenage mothers while these birth weights tended to be higher among adult mothers. For example, about one third of teenage mothers (33.9%) gave birth to babies with low birth weight (<2.5 Kg) compared to only one tenths of adult mothers (10.2%) giving birth to babies with low birth weight (P<0.001). Considerably more babies born to teenage mothers (33.9%) were admitted to NICU than those born to older women (11%), (P<0.001). Stillbirth was not significantly different between the two groups (P=0.066).

Table 1: Comparison of teenage and adult mothers according to different background characteristics

<table>
<thead>
<tr>
<th></th>
<th>Teenage mothers</th>
<th>Adult mothers</th>
<th>Total (n=236)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (n=118)</td>
<td>% (n=118)</td>
<td></td>
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</tr>
<tr>
<td>Area of residence</td>
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<tr>
<td>Khartoum State</td>
<td>70.4</td>
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<td>Outside Khartoum State</td>
<td>29.6</td>
<td>17.8</td>
<td>56</td>
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<tr>
<td>Level of education</td>
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<td></td>
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</tr>
<tr>
<td>Illiterate</td>
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<td>16.9</td>
<td>50</td>
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<td>Primary school</td>
<td>26.3</td>
<td>18.6</td>
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<tr>
<td>Secondary+</td>
<td>48.3</td>
<td>64.4</td>
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<tr>
<td>Socio-economic level</td>
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<tr>
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<tr>
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<td>13.6</td>
<td>11.9</td>
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</table>

*Fisher exact test*
Maternal pregnancy outcomes are presented in Table 3. Significantly more teenage mothers (14.4%) had higher blood pressure of 140-159 / 90-109 mm Hg compared to adult mothers (6.8%), (P=0.014). And more profoundly about 6-fold teenage mothers (6.0%) had blood pressure ≥160/110 mm Hg than adult mothers (0.8%).

Although more teenage mothers had instrumental delivery (3.4%) or Caesarean sections (17.8%) than adult mothers who had 1.6% and 10.2% of their babies delivered with instrumental delivery or Caesarean sections respectively, this difference was not statistically significant (P=0.139). Postpartum haemorrhage was found in; 6.8% of the adult mothers compared to 1.6% of teenage mothers (P=0.053). Prevalence of anemia, antepartum hemorrhage, duration of labour, mode of delivery and stillbirths were not significantly related to maternal age at delivery.
Table 3: Comparison of teenage and adult mothers according to maternal pregnancy outcomes

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<tr>
<th>Outcomes</th>
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<th>Adult mothers (n=118)</th>
<th>Total (n=236)</th>
<th>p-value</th>
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<tbody>
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<td></td>
<td></td>
<td></td>
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<td>92.4</td>
<td>203</td>
<td>0.014</td>
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<td>14.4</td>
<td>6.8</td>
<td>25</td>
<td></td>
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<td>≥160/110</td>
<td>6.0</td>
<td>0.8</td>
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<tr>
<td>Haemoglobin concentration in gm/dl</td>
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<td>8.8</td>
<td>13.8</td>
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</table>

*Fisher exact test
Discussion

This study found significantly higher proportion of teenage mothers had no antenatal care visits during this pregnancy than adult mothers. Scholl et al.\(^{(18)}\) found a higher proportion of teenage mothers booked after 20 weeks gestation. These results indicated that teenager mothers in this study might have been reluctant to seek medical advice probably due to residing outside the capital city (\(P=0.032\)), they had lower level of education (\(P=0.044\)) and lower socioeconomic status (\(P<0.001\)).

In this study 14.4% and 6% of teenage mothers had statistically significant high blood pressure of 140-159/90-109 mm Hg and \(\geq160/110\) mm Hg compared to 6.8% and 1% of adult mothers respectively (\(P=0.014\)). Konje et al\(^{(19)}\) found increased risk for hypertension in adolescents but no difference in pre-eclampsia. Adedoyin and Adetoro\(^{(20)}\) found decreased risk for hypertension and more for pre-eclampsia. Treffers et al\(^{(21)}\) commented that there seemed to be discrepancy between the incidence of hypertensive disorders among pregnant adolescents in different countries. These results are in line with the reports mentioned in the literature and raise the implication of the length of sexual cohabitation before conception and this was not applicable to the situation of this study.

Postpartum haemorrhage was statistically significantly increased among adult mothers (6.8%) versus (1.6%) teenage mothers (\(P=0.053\)). This was found by Jolly et al.\(^{(22)}\) which can be explained by better myometrial function in the younger group.

Despite statistically significant differences in areas of residence, level of education and socioeconomic status among the study population, anaemia (haemoglobin level less 11 g/dl according to WHO definition\(^{(23)}\)) among teenage and adult mothers was 35.6% and 36.4% respectively. These percentages were not statistically significant (\(P=0.892\)). Scholl et al.\(^{(18)}\) reported no statistically significant difference in the prevalence of anaemia between the two groups although de Vienne et al.\(^{(24)}\) reported 1.27 relative risk of anaemia for younger women. The incidence of anaemia is so high in all women in developing countries which may explain the small difference of anaemia between teenage and adult mothers. The cause of anaemia is not the young age of the pregnant woman. Anaemia in pregnancy is often caused by nutritional deficiencies, malaria and hookworms infestation in developing countries.

Low birth weight was significantly higher among teenage (33.9%) than in adult mothers (10.2%), (\(P<0.001\)). Similar results were obtained by Prianka et al.,\(^{(13)}\) Leland et al.\(^{(25)}\) and Fraser et al.\(^{(26)}\) In these studies, this may be due to preterm delivery and hence low birth weight in the younger age group where gestational age was considered. The situation may be different in the present study since gestational age at delivery was not taken to draw such conclusion, but the higher blood pressure among teenage mothers may in part be an explanation of this lower birth weight.

Lower Apgar score (<5) was significantly more prominent among newborns of teenage mothers (17.8%) compared to adults (6.0%) (\(P=0.005\)). This may be due to the low birth weight found among newborns of teenage mothers. The significantly higher blood pressure may be a reason, by causing placental insufficiency. Labour duration or mode of delivery did not differ significantly in the two groups and cannot explain this low Apgar Score.

The highly significant increased risk in the admission of the newborn to the NICU among teenage mothers (33.9%) compared to 11.0% among adult mothers (\(P<0.001\)) may be due to low birth weight and/or prematurity of the newborn. The study did not find an increased risk of stillbirth among teenage mothers (\(P=0.066\)). Bradford & Giles\(^{(27)}\) found the same result contrary to de Vienne et al.,\(^{(24)}\) Ward & Bigg\(^{(28)}\) & Rahman et al.\(^{(29)}\) who found increased risk of stillbirth among teenage mothers.

Conclusion

Teenage pregnancy carries high risk to the mother and newborn compared to adult mothers.

References


2. United Nations Population Fund. Adolescents in India. A profile, a publication of the UN Inter


22. Jolly MC, Sebire N, Harris J, Robinson S, Regan...


Seroprevalence of celiac disease in Sudanese children: A retrospective study
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2Department of Pediatrics, Faculty of Medicine, University of Khartoum, Khartoum-Sudan.

Abstract

Objectives: To investigate the prevalence of seropositivity of celiac disease (CD) in Sudanese children who presented with clinical features suggestive of the disease.

Methods: This is a retrospective hospital-based study. Sera from 205 Sudanese children (105 males and 100 females) of two age groups (< 10 years and 10-20 years) were analyzed for anti-tissue transglutaminase (anti-tTG) IgG and IgA autoantibodies using a commercial indirect ELISA (iELISA) kits, after obtaining informed verbal consent from the parents or caregivers.

Results: Fifty six out of 205 children (27.3%) were seropositive for (anti-tTG) IgG and IgA autoantibodies. Among them, 30 (53.6%) were females and 26 (46.4%) were males. Out of the 205 children, 84 (41%) had type 1 diabetes mellitus (DMI) and among them 7 (8.3%) were seropositive for anti-tTG IgG and IgA autoantibodies. No statistically significant difference (P=0.06) was observed in the CD patients between the two age groups. Varying frequencies of symptoms and signs in those who were positive CD serology was observed with high prevalence of diarrhea (32.1%).

Conclusions: Our findings show that CD seroprevalence in Sudanese children with clinical features suggestive the disease was high (27.3%). Females were affected more than males. The seroprevalence of CD among children with type 1 diabetes mellitus (DM1) was 8.3%.

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Introduction

Celiac disease (CD) is an immune mediated enteropathy initiated by ingestion of gluten, in genetically susceptible individuals(1). It is characterized by lifelong intolerance to gluten, which is a mixture of gliadin and related prolamine present in cereals such as wheat, barley and rye. It was initially believed to be a disease predominantly affecting the European population but the highest prevalence of 5.6% which was reported in the Saharawis of the Arab-Berber origin living in the Sahara desert, is almost 10 fold higher than that reported from most European countries(1). Over the last decade with availability of more sensitive and specific diagnostic tools, the epidemiology has changed with more cases of CD being reported from other parts of the world. The prevalence of the disease ranging from 0.6 to 0.8 in the Middle East is almost similar to that of Europe (2). In African populations, specifically in the Meghreb area (the Northern Region of Africa including Morocco, Algeria, Tunisia, Libya and Egypt) very high incidences of CD have been reported both in general population (3) and at risk-groups (4). The disease was first reported from Sudan in 1978 (5). Mohammed et al. (6) reported that the prevalence of CD in selected high-risk Sudanese children was 22.5% (18/80) using anti-gliadin autoantibodies (AGA-IgA and IgG), endomysial antibody (EMA) and confirmatory biopsies. The diagnostic gold standard for CD has long been considered to be intestinal biopsy; it is impractical to perform this invasive and costly procedure on all at-risk individuals. Instead, in a recent technical review of American Gastroenterological Association (AGA) recommended that these individuals should first be screened for CD with IgA- anti-tissue Transglutaminase (tTG) serology (7). Given its high sensitivity and specificity, a negative tTG
may effectively rule out CD, where a positive tTG may identify those who warrant an intestinal biopsy to confirm CD. Recent study reported that high tTG antibody level (5-folds the upper limit of normal) is 100% specific for duodenal atrophy in adult patients at high risk of CD (8). Additionally, the AGA states that physicians may consider screening tTG-negative patients for IgA deficiency (3% of CD patients are IgA deficient and therefore IgA tTG negative) (9). Double positive test results (IgA anti-tTG and IgG anti-deamidated gliadin (DGP) had the highest likelihood ratio for CD, whereas double negative test results had the lowest likelihood ratio (10).

In an attempt to investigate the seroprevalence of CD in Sudanese children who presented with clinical features suggestive of the disease, herein study was conducted using a serological test as initial screening tool and to determine the prevalence of seropositivity of the disease among children with symptoms including children with type 1 diabetes mellitus.

Material and Methods
Study design
This is a retrospective hospital-based study ran from July 2007 to September 2009 in the main pediatric hospital in Khartoum State (Gaffar Ibn Oaf children hospital).

Patients and Methods
Sera were collected from 205 children (105 males and 100 females) of two age groups (<10 years and 10-20 years) who presented with two or more of the following: chronic diarrhea, growth retardation, weight loss, unexplained iron deficiency anemia or family history of CD. Informed verbal consent was obtained from the parents or caregivers. The data were collected with a predesigned questionnaire giving information about age, gender, tribe, clinical symptoms and signs and whether patient was diabetic or not.

Measurements
Anti- tissue Transglutaminase (anti-tTG) IgG and IgA measurement
Commercial indirect ELISA (iELISA) kits of anti-tTG IgG and IgA were purchased from Orgentec Diagnostika GmbH (ORG, Germany). Positive serum samples will present yellow colour. The colour visualized in each well is proportional to the titre of human’s antibody specific to tissue Transglutaminase present in the diluted sample (1/100). The test is based on the principle of an indirect ELISA in which plates are coated with human recombinant tissue Transglutaminase. Test sera are applied and specific antibodies bind to respective antigen is then detected with horseradish peroxidase (HRP) anti-human IgG and IgA conjugate and substrate. The reaction was stopped by adding stop solution (IM HCl). Finally, the optical density (OD) was measured using microplate reader instrument (Expert Plus, EC) at 450 nm with a reference at 620 nm. The mean absorbance for each set of duplicate calibrators, controls and patients sera was calculated. The antibody concentration of unknown was determined from standard curve. The cutoff value of antibody titre is ≥ 15 i.e. all samples, which have antibody titre ≥ 15, are considered positive.

Data analysis
Data were analyzed by SPSS software package (version 13.0 windows) using Pearson chi-square test with p 0.05 being level of significance.

Results
The prevalence of anti-tTG IgG and IgA (≥15 IU/ml) among 205 children with clinical features suggestive of the disease was 27.3% (56/205). Among positive anti-tTG IgG and IgA children, 30 (53.6%) were females and 26 (46.4%) were males. In the present study out of 205 children, 84 (41%) had type 1 diabetes mellitus (DM1) and among them 7 (8.3%) were seropositive for anti-tTG IgG and IgA. No statistical significant difference (P=0.06) was observed in CD between two age groups (Table 1). Children descending from Arab tribes were affected more often than others (data not shown). Varying prevalence of symptoms and signs in positive CD serology was observed with high prevalence of diarrhea (32.1%) (Table 2).
Celiac disease (CD) was first reported from Sudan in 1978 when 7 children were diagnosed by intestinal biopsy (5). Thereafter, Mohammed et al. (6) recorded a prevalence of 22.5% (18/80) of CD in Sudanese children using intestinal biopsy and a prevalence 38% and 55% using anti-gliadin antibodies (AGA) and endomysial antibodies (EMA), respectively. In this study screening human sera samples collected from 205 Sudanese children for anti-tTG IgG and IgA showed prevalence 27.3% (56/205) of seropositivity of CD.

The prevalence of seropositivity of CD in Sudanese children reported in the current study (27.3%) is much higher than that reported in Iran (6%) (11) and lower than that recorded in Libya (31.6%) (12), India (54.6%) (13) and Argentina (33.1%) (14).

A strong association between DMI and CD is well documented (15), as the prevalence of CD in DMI patients can be up to 20 times higher than that of healthy population (16). In the present study DMI patients were screened for anti-tTG IgG and IgA antibodies either as a routine test in the onset of the disease or according to suspected celiac symptoms noticed by the physician in DMI subjects. In this study, 7 out of 84 (8.3%) children with type 1 diabetes mellitus (DM1) were seropositive for anti-tTG IgG and IgA. This is in concordance with the seroprevalence (7%) of CD in type 1 diabetes mellitus using anti-tTG IgA reported in Sudanese children (personal communication). The slight difference in the prevalences between the two studies may be due to that 3% of CD patients are IgA deficient and therefore anti-tTG IgA is false-negative (9). In order to avoid false-negative results in patients with selective IgA deficiency it is recommended to measure total IgA. A second drawback of the detection of IgA anti-tTG is that hemolysis can cause false-negative results by sequestration of anti-tTG antibodies, especially in patients with low IgA anti-tTG titers (17).

The seroprevalence of 8.3% CD in Sudanese diabetic children detected in this study is similar to seroprevalence that was reported in Tunisian diabetic patients (18). It is lower than that reported in Mexico (19) and higher than those in European countries (20) and Iranian diabetic children (21). However, it should be emphasized that celiac serology may fluctuate in DM1. Initial negative serology does not rule out CD, as almost 40% of patients develop CD a few years after onset diabetes. Similarly, transient false positive serology is also known in DMI (22).

In the present study, the prevalence of CD in females {53.6% (30/56)} is higher than in males {46.4%}

<table>
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<tr>
<td>Diarrhea</td>
<td>18 (32.1)</td>
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<tr>
<td>Growth retardation</td>
<td>10 (17.9)</td>
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<td>Vomiting</td>
<td>7 (12.5%)</td>
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<tr>
<td>Weight loss</td>
<td>3 (5.4%)</td>
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</tbody>
</table>

Discussion

Table 1: Influence of age groups on seroprevalence of CD in Sudanese children.

Table 2: Frequency of presenting features in positive CD serology in Sudanese children.(n=56)

Celiac disease (CD) was first reported from Sudan in 1978 when 7 children were diagnosed by intestinal biopsy (5). Thereafter, Mohammed et al. (6) recorded a prevalence of 22.5% (18/80) of CD in Sudanese children using intestinal biopsy and a prevalence 38% and 55% using anti-gliadin antibodies (AGA) and endomysial antibodies (EMA), respectively. In this study screening human sera samples collected from 205 Sudanese children for anti-tTG IgG and IgA showed prevalence 27.3% (56/205) of seropositivity of CD.

The prevalence of seropositivity of CD in Sudanese children reported in the current study (27.3%) is much higher than that reported in Iran (6%) (11) and lower than that recorded in Libya (31.6%) (12), India (54.6%) (13) and Argentina (33.1%) (14).

A strong association between DMI and CD is well documented (15), as the prevalence of CD in DMI patients can be up to 20 times higher than that of healthy population (16). In the present study DMI patients were screened for anti-tTG IgG and IgA antibodies either as a routine test in the onset of the disease or according to suspected celiac symptoms noticed by the physician in DMI subjects. In this study, 7 out of 84 (8.3%) children with type 1 diabetes mellitus (DM1) were seropositive for anti-tTG IgG and IgA. This is in concordance with the seroprevalence (7%) of CD in type 1 diabetes mellitus using anti-tTG IgA reported in Sudanese children (personal communication). The slight difference in the prevalences between the two studies may be due to that 3% of CD patients are IgA deficient and therefore anti-tTG IgA is false-negative (9). In order to avoid false-negative results in patients with selective IgA deficiency it is recommended to measure total IgA. A second drawback of the detection of IgA anti-tTG is that hemolysis can cause false-negative results by sequestration of anti-tTG antibodies, especially in patients with low IgA anti-tTG titers (17).

The seroprevalence of 8.3% CD in Sudanese diabetic children detected in this study is similar to seroprevalence that was reported in Tunisian diabetic patients (18). It is lower than that reported in Mexico (19) and higher than those in European countries (20) and Iranian diabetic children (21). However, it should be emphasized that celiac serology may fluctuate in DM1. Initial negative serology does not rule out CD, as almost 40% of patients develop CD a few years after onset diabetes. Similarly, transient false positive serology is also known in DMI (22).

In the present study, the prevalence of CD in females {53.6% (30/56)} is higher than in males {46.4%}
(26/56). This is in agreement with Al-Tawaty and Elbargathy (12).

No statistical significant difference ($P=0.06$) was observed in CD between the two age groups. This may be attributed to the fact that CD is diagnosed typically in early childhood around age of 2 years and a second peak is found around age of 40 years. (23)

It could be concluded that CD seroprevalence in Sudanese children with clinical features suggestive the disease was high (27.3%). Moreover, females were affected more than males. Children with type 1 diabetes mellitus (DM1) presented with CD with seroprevalence of 8.3%. No statistical significant difference was observed in CD between two age groups.

It was recommended that the prompt and accurate diagnosis of CD is essential, as it requires lifelong adherence to gluten free diet (GFD). Although commercially available tTG screening tests based on human purified or human recombinant as antigen have sensitivity and specificity greater than 90% (24), a confirmatory small intestinal biopsy is recommended to confirm CD diagnosis because of the risk of false-positive tTG results. Early diagnosis and treatment have additional benefits because studies suggest that delayed diagnosis is associated with increased prevalence of other autoimmune conditions (25), mortality (26) and increased risk of osteoporosis and malignancies (27). It is therefore imperative to have standardized protocols using sensitive and specific tests that can confirm the diagnosis of CD and identify individuals at risk.

**Acknowledgment**

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**References**


Introduction: Congenital dislocation of the knee (CKD) is a rare congenital anomaly which was first reported in 1822, with a reported incidence of 1:100,000 life birth, it is much less common compared to Developmental Dysplasia of the Hip (DDH) and Congenital Talipes Equino Varus (CTEV). Females are more prone to be affected by the disease. It can occur either alone or as part of other anomalies. The condition is thought to be due to failure of internal rotation of the myotome of the femur and quadriceps muscle.

Objective: to study outcome of management of Congenital Knee Dislocation (CKD) at Soba University Hospital.

Methods: Retrospective review of records of patients of congenital knee dislocation in the Department of Paediatric Orthopaedics, Soba university Hospital. All patients were included, their demographic characteristics were studied. Classification of severity was according to Leveuf and Pias. The assessment of the outcome of management was based on range of movement, stability and absence of pain.

Results: Twenty eight patients, 17 females and 11 males, with ages ranging between two days and 8 years with a median age of 1.5 months. It was unilateral in 12 patients and bilateral in 16 patients (44 knees). In 65% of patients it was an isolated abnormality. In over 55% of cases the dislocation was grade III. Both conservative and operative management were performed almost in equal numbers. The outcome was good in 90% of cases. Conservative treatment give better outcome than operative treatment.

Conclusion: Early presentation at an age less than three months and conservative management are associated with better outcome.

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Objectives
To study the demographic characteristics, the clinical pattern and outcome of management of patients with congenital knee dislocation seen at the paediatric Orthopaedic Department, Soba University Hospital.

Methods
This is a retrospective study. The hospital records of patients who presented to the Paediatric Orthopaedic Department at Soba University Hospital(SUH) with knee problems between the years 2000 and 2010 were reviewed. Demographic data of patients, patterns of presentations as well as management and outcome of treatment were reviewed. Classification of CKD was according to that reported by Leveuf and Pais(17) which is now widely accepted. This classification is based on the range of passive flexion; Grade I; Simple genu recurvatum with range of passive flexion(ROF) more than 90 degrees, Grade II; Subluxation with ROF between 30 and 90 degrees, Grade III; Dislocation with ROF less than 30 degrees (12).

Conservative treatment was offered to all patients who presented early; less than 1 month (12). Operative treatment was indicated whenever conservative treatment with physiotherapy failed (18), and when the condition was part of multiple anomalies as in arthrogryposis(9) or in very severe cases. (19)

Surgical treatment involved lengthening of the quadriceps tendon with a V-Y plasty enlarging the supra-patellar pouch by anterior capsulotomy, IT band and lateral release. (16) In this series 21 knees out of 44 were treated conservatively.

Outcome assessment was evaluated labelling an excellent outcome; when the knee function had a full range of flexion, stable and painless motion. Good; with a flexion to 90° or more with slight instability or pain; fair, with flexion of 45 to 90° with mild instability or pain. It is labelled poor when flexion is less than 45° with gross instability and pain (16).

Results
During the study period, 84 patients with different knee deformities presented to the SUH paediatric orthopaedic clinic. Congenital knee dislocation comprised almost one third of knee deformities; 28 out of 84 patients (33.34%) and 44 knees. Of the 28 CKD patients 8 were males and 20 were females, their ages ranged between two days and 8 years(Table 1), with a median age of 1.5 months. The dislocation was bilateral in 16 patients, and unilateral in 12 patients(six on the right and six on the left knees); a total of 44 knees.

<table>
<thead>
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<th>Age Range</th>
<th>Number of Patients</th>
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<td>&lt; 1 month</td>
<td>10(35.71%)</td>
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<td>1 - 4</td>
<td>7(25%)</td>
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<tr>
<td>5 – 9</td>
<td>2(7.14%)</td>
</tr>
<tr>
<td>10 – 14</td>
<td>2(7.14%)</td>
</tr>
<tr>
<td>15 – 19</td>
<td>1(3.55)</td>
</tr>
<tr>
<td>20 – 24</td>
<td>2(7.14%)</td>
</tr>
<tr>
<td>&lt; 25</td>
<td>4(14.29%)</td>
</tr>
<tr>
<td></td>
<td>28(100%)</td>
</tr>
</tbody>
</table>

It was associated with other abnormalities in 10 patients (35.7%) (Table 2). Of the 44 dislocated knees, 25 knees were grade II, nine were grade I and ten were grade III (Table 3). 21 knees (47.8%) were treated conservatively and 20 knees (45.5%) were treated operatively. One patient -with one knee- (2.3%) was awaiting the surgery at the time of the study and one patient with bilateral CKD was lost during follow up. The outcome was good in 39 knees (95.12%), fair in 2 (4.88%) (Table 4).

<table>
<thead>
<tr>
<th>Associated Anomaly</th>
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<td>DDH</td>
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<td>CTEV</td>
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<tr>
<td>Spina Bifida</td>
<td>2</td>
</tr>
<tr>
<td>Absent patella</td>
<td>1</td>
</tr>
<tr>
<td>TibialHemimelia</td>
<td>1</td>
</tr>
<tr>
<td>PesPlanus</td>
<td>1</td>
</tr>
<tr>
<td>Mental Retardation</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Degree of CDK</th>
<th>No. of Knees &amp; %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>9(20.46%)</td>
</tr>
<tr>
<td>Grade II</td>
<td>25(56.81%)</td>
</tr>
<tr>
<td>Grade III</td>
<td>10(22.73%)</td>
</tr>
<tr>
<td>Total</td>
<td>44(100%)</td>
</tr>
</tbody>
</table>
Table 4: Functional outcome, related to modality of treatment, (n=41 knees).

<table>
<thead>
<tr>
<th>Functional outcome</th>
<th>Number of Knees</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Conservative</td>
</tr>
<tr>
<td>Good</td>
<td>21</td>
</tr>
<tr>
<td>Fair</td>
<td>--</td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
</tr>
</tbody>
</table>

Discussion
Congenital knee dislocation is a rare condition \(^2\) that can be isolated or associated with other anomalies. In this series it comprised one third of paediatric knee problems who presented during the study period. Prevalence was 2.86% of all patients presenting at the paediatric orthopaedic department at Soba University Hospital during the period 2000 – 2010 yrs.

Twenty-eight patients (44 knees) were reviewed. The commonest age at presentation was two days, which reflects that the disorder is usually presented at birth, a similar finding was reported by Herring \(^{20}\) and many other authors.\(^{6,11,21,22}\) In common with the known trend, female predominance was found in the present series (60.7%), in many studies females were found to be as twice as males\(^{6,22}\).

In the present series no patient had family history of the knee disorder indicating rarity of inheritance or genetic base of the disease; Provanzo\(^{23}\) reported a similar finding reviewing 200 patients with CDK only seven patients had family history. Curtis and Fisher \(^{22}\) described “heritable congenital tibio-femoral subluxation, a genetically transmitted syndrome where CDK is associated with abnormalities in the face and spine. None of our patients had abnormalities in the face and spine.

The condition was bilateral in over half of our series; similar to the finding was reported by Martin\(^9\). Associated anomalies were found in 82% of the series reported by Katz\(^1\). In this current series, associated anomalies were found in 12 patients (43%). In both series the commonest were DDH and CTEV.

Grade II was the commonest type; it amounted to over 55% of our series (25 out of 44 knees). A similar finding was reported by Abdelaziz\(^{12}\).

Based on the fact that late presentation necessitates proceeding to surgical release without trial of conservative measures\(^{24}\), six patients were operated on without conservative trial and 2 of them had fair outcome.

Based on Ferris\(^{16}\) classification of outcome of treatment, in the current series, thirty nine knees (95.1%) had a good functional outcome, 2(4.9%) had fair and none had poor function. Many authors\(^{16,19}\) reported excellent outcome, we did not have excellent outcome in our series, probably due to poor postoperative physiotherapy services which were practiced in different centres as patients were from different parts of Sudan.

In the current series, good treatment outcome was found to be associated with conservative treatment and early presentation; almost all those who were younger than 4 months at presentation and all those who were treated conservatively had good outcome.

Conclusion
Conservative treatment in patients presenting early (less than 4 months) is associated with good outcome.

References

Outcome of management of congenital knee dislocation at Soba University Hospital
Outcome of ischemic diabetic foot in Jabir Abu Eliz Diabetic Centre, Khartoum
ELTahir Ahmed ELTahir¹, Mohamed ELMakki Ahmed²*
¹Jabir Abu Eliz Diabetic centre, ²University of Khartoum

Abstract
Background: Diabetes Mellitus contributes to a number of disorders that can affect the quality of life. Both the risk of extremities amputation and mortality are much increased in case of peripheral vascular disease. The aim of the study is to report on the outcome of diabetic patients with lower limb ischemia attending Jabir Abu ELiz Diabetic Centre, (JADC) Khartoum.

Methods: This is a prospective cross sectional hospital based study done in JADC in the period from 1st of September 2010 to July 2011. All patients with diabetic ischaemic foot referred to the vascular surgeon for assessment and possible intervention were included. All patients were followed for 10 months after being referred to the vascular surgeon.

Results: There were a hundred diabetic patients with ischemic foot, 72 patients were males, and 28 patients were females, with male to female ratio 2:6:1:0. The mean age ± SD was 62.5±11 years and the age ranged between 38-90 years. Thirty seven patients ended with lower extremity amputation (LEA), twenty four patients (44%) had their wounds healed without amputation and 19 patients continued to have persistent ulcer. Patients younger than 70 years, those with ulcer duration< 6months and ABPI0.5<, had their ulcers healed significantly more compared to the counterparts (24vs19). Patients who had Major Lower Extremity Amputation (LEA) were significantly older with an ulcer more than 6 months duration and Ankle Brachial Pressure Index (ABPI) less than 0.5. Death was reported in 8 patients. Sex, duration of diabetes, smoking and hypertension did not affect outcome.

Conclusion: Diabetic ischemic foot had a high risk for major LEA. Older age, significant lower limb ischemia and an ulcer of prolonged duration were significant contributing factors.

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Introduction
Diabetics, with Chronic Limb Ischemia (CLI); have a 34% risk for amputation, compared to only 8% in non diabetic persons.¹²

Despite the myriad of studies done in the industrialized countries for lower limb ischemia in diabetes, there were few publications from the African continent ². The aim of this study is to report on the outcome of diabetic patients with lower limb ischemia seen by an attending consultant surgeon in JADC and referred to the vascular surgeon.

Patients and methods
All patients with ischemic diabetic feet referred by the attending consultant surgeon to vascular surgeons were studied. Clinical data were recorded in a specially designed sheet. This included clinical evaluation ie the patient’s age, sex, type and duration of DM, the method of control of DM, smoking and its duration, previous foot lesion and hypertension.

The vascular assessment included history of claudication and rest pain, examination of the pulses, skin abnormalities and skin temperature. The limb circulation was assessed using Doppler examination and calculation of the ankle brachial pressure index (A/BPI) using the standard procedure. Peripheral vascular disease was defined by an ankle/brachial pressure ratio; normal value is >0.9 – 1.4, borderline between 0.9 – 0.5 and critical ischaemia<0.5.

Invasive femoral angiography and CT angiography were done when appropriate. Patients who needed amputation were referred to the emergency department in the main hospitals.

Data were analyzed using computer statistical professional software package programme of data analysis. (SPSS) version 18. Both dependent and
independent variables were displayed as frequency tables and figures.

**Results**

A hundred patients with ischemic diabetic foot were studied, 72 were males and 28 were females, giving a male to female ratio of 2.6:1.0. The mean age ± SD was 62.5±11 years and the age ranged between 38-90 years. Thirty two patients (32%) were between 61-70 years of age.

Sixty patients (60%) had diabetes for more than 15 years, and 6 patients (6%) had diabetes for less than 5 years. Sixty four patients were on oral hypoglycaemic drugs, 32 on insulin and 4 on both oral hypoglycaemic drugs and insulin.

Thirty seven patients (37%) were hypertensive and 12 patients were smokers (12%). Seventy four patients presented with foot ulceration, 22 with pain and 18 patients with gangrene. Table 1 shows A/BPI in all patients.

Table 1 ABPI in the diseased and contra lateral legs in diabetic patients with lower limb ischemia

<table>
<thead>
<tr>
<th>ABPI</th>
<th>Posterior tibial artery</th>
<th>Dorsalis pedis artery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Diseased leg</td>
<td>Contra lateral leg*</td>
</tr>
<tr>
<td>&lt;0.5</td>
<td>28</td>
<td>0</td>
</tr>
<tr>
<td>0.5-0.9</td>
<td>64</td>
<td>8</td>
</tr>
<tr>
<td>0.9-1.2</td>
<td>-</td>
<td>71</td>
</tr>
<tr>
<td>&gt; 1.2</td>
<td>8</td>
<td>7</td>
</tr>
</tbody>
</table>

missing data * 14

** 14

Twenty four patients had previous major LEA. Forty three patients were predominantly with ischemic feet and fifty seven had neuroischemic feet. Table 2 shows the outcome for all 100 patients.

Table 2 Outcome of all 100 diabetic patients with lower limb ischemia after 10 months follow up

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major amputation</td>
<td>37</td>
<td>37%</td>
</tr>
<tr>
<td>Persistent ulcer</td>
<td>19</td>
<td>19%</td>
</tr>
<tr>
<td>Healed ulcer</td>
<td>13</td>
<td>13%</td>
</tr>
<tr>
<td>Healed ulcer with Minor amputation</td>
<td>11</td>
<td>11%</td>
</tr>
<tr>
<td>Granulating wound</td>
<td>6</td>
<td>6%</td>
</tr>
<tr>
<td>Persistent pain</td>
<td>3</td>
<td>3%</td>
</tr>
<tr>
<td>Improved pain on walking</td>
<td>3</td>
<td>3%</td>
</tr>
<tr>
<td>Death</td>
<td>8</td>
<td>8%</td>
</tr>
</tbody>
</table>
Thirty seven patients underwent major LEA including those following vascular surgical intervention (n=4), 36 of them had trans-tibial amputation and one had transfemoral amputation. Twenty four were males and 13 were females.

Table 3 Factors related to amputation in diabetic patients with lower limb ischemia

<table>
<thead>
<tr>
<th>Factors</th>
<th>Amputee (n=37)</th>
<th>Non amputee (n=63)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ulcer duration &gt;6m</td>
<td>29</td>
<td>24</td>
<td>0.00</td>
</tr>
<tr>
<td>ABPI &lt; 0.5</td>
<td>21</td>
<td>7</td>
<td>0.02</td>
</tr>
<tr>
<td>Age &gt; 70 years</td>
<td>20</td>
<td>35</td>
<td>0.03</td>
</tr>
<tr>
<td>Duration of diabetes &gt; 10 years</td>
<td>30</td>
<td>46</td>
<td>0.2</td>
</tr>
<tr>
<td>Hypertension</td>
<td>12</td>
<td>25</td>
<td>0.1</td>
</tr>
<tr>
<td>Pain</td>
<td>6</td>
<td>15</td>
<td>0.2</td>
</tr>
<tr>
<td>Gangrenous toes</td>
<td>7</td>
<td>11</td>
<td>0.2</td>
</tr>
<tr>
<td>Smoking</td>
<td>4</td>
<td>8</td>
<td>0.3</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>8</td>
<td>-</td>
</tr>
</tbody>
</table>

Sixty three patients (63%) didn’t have major amputation, 48 patients were males and 15 were females. In those latter group forty patients were on oral hypoglycaemic drugs and 20 on insulin, while 3 patients on both. Forty five patients presented with ulcer, 15 patients with pain at rest, two with claudication and 11 patients with gangrene. Twenty five patients were hypertensive and 8 were smokers. Ulcer healing significantly increased with age >70 yrs, A/BI index >0.5 and ulcers of < 6 months duration.

The total mortality in the present series was 8 patients. Six of them died at home and no clear diagnosis was established, one due to severe sepsis and one had femoropopliteal bypass and never recovered from anesthesia. Six of the deaths were males and two were females their age ranged between 55-75 years. Three of them were smokers and one was hypertensive. Three of them had previous lower limb major amputation.

Discussion
A total of 100 diabetic patients with lower limb ischemia were studied. Males were affected more than females with a ratio of 2.6:1.0. Similar sex ratio was reported (3,4,5). Most of our patients were in the age group 61-70 years with a mean age of 62.5±11 years as was reported previously from JADC (6).

We report a rate of lower extremity amputation (LEA) of 37%. A similar rate was reported on diabetic patients with severe sepsis in Khartoum Teaching Hospital (KTH)(7). A higher rate of 60% was reported from KTH in 1995 (8). A previous rate of 29% amputation in JADC was reported among all diabetic patients of whom 61% were due to lower limb ischemia (6). The overall amputation rate in JADC during the last two years has been 12-14 %.

Regionally few references are found regarding to LEA in diabetic patients with lower limb ischemia. In Tanzania, the amputation rate in patients with diabetic foot and PVD was 47%.(1)

Corresponding rates in Europe were relatively low, as interventional therapeutic modalities both operative and non operative were being widely used. Faglia etal (9) reported 5% LEA in diabetics with major lower limb ischemia. This can partly be explained by the fact
that diabetic patients in Western communities are more compliant with treatment. They are more educated and have access for vascular intervention in the form of angioplasty or bypass resulting in substantial reduction (50-90%) in the rate of amputation.\(^{(10)}\)

Twenty one patients (56%) who had major LEA amputation had A/BPI less than 0.5. Reiberet al found an increased risk of amputation, if ABPI was less than 0.5.\(^{(11)}\)

A study of the vascularhistopathological changes in diabetic patients from JADC, who had LEA reported histological evidence of atherosclerosis in 99% of all specimens.

A study from the same centre (JADC) reported that a chronic ulcer for more than 6 months is a risk factor for major LEA\(^{(12)}\). Oyibo et al\(^{(13)}\) showed that ischemic/neuroischemic ulcers had a longer median healing time (20 vs. 9 weeks), and were three-times more likely to lead to an amputation (23.5 vs. 10%), compared to neuropathic ulcers.

In patients with A/BPI <0.9 we report 41% (n=24) healing rate. This is lower than the international data where the healing rate range between 73-95%, following angioplasty and/or reconstructive vascular surgery.\(^{(9,14)}\)

Twenty four patients who showed primary healing had ABI >0.5, twenty one patients of them (88%) were below 70 years, and all had ulcer duration of < 6 months. Jan Apelqvist\(^{(15)}\), in a similar study, reported a healing rate of 72%; the main predictors of healing were age <75, ABPI >0.5 and severity of ulcer (single ulcer, Wagner class1&2).

**Conclusion**

Ischemic diabetic foot is a real challenge to both general and vascular surgeons. Foot ulceration was the leading cause for consultation in Jabir Abu Eliz Diabetic Center.Khartoum. Older age, severity of PVD and ulcer duration were the predictors of outcome.

**References**

Night calls between resting the muscles and avoiding the mental hassle

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Department of Medicine, University of Khartoum. drtarawa1@hotmail.com

Abstract
It is well documented that night shift is associated with increased medical and surgical errors due to decreased vigilance and cognitive reasoning during night calls. In this paper we examined the readiness of junior doctors to cope with extended night calls. It seemed that half of our junior doctors lack the abilities to cope well with night calls. They were unprepared to handle call nights both efficiently and safely. This calls for a formal orientation and monitoring by the employers to enhance both patients’ safety and doctors’ professional well being.

Introduction
Illnesses do occur during days and nights, this is why medical practitioners are obliged to have some of their services available around the clock. It is estimated that 27% of US work force work nights permanently or on rotating shift (1). Our bodies are programmed to stay awake at daytime and sleep at night that is why working night shifts is a direct cause of sleep deprivation and fatigue. It is well documented that night shifts are associated with increased medical and surgical errors due to decreased vigilance and cognitive reasoning during night calls (2). It reduces the psychomotor performance to someone with blood alcohol level of 0.10 % (3) which is more than the current legal maximum limit for driving in UK (0.08%). It also increases the risk of being involved in road traffic accidents on the way home. Both employers and doctors have a professional obligation to minimize risks during night shifts through implementing appropriate working hour schedules and making sure one is rested and refreshed before coming on duty. This includes being ready mentally, physically and psychologically to ensure an optimal service for patients and better standards of safety for both patients and doctors (4).

In this paper we examined the readiness of our junior doctors to cope with extended night calls. To our knowledge this paper is the first attempt to examine the pattern of preparation, tolerance and recovery from night calls amongst junior Sudanese doctors aiming to get a deep understanding of their attitude towards this difficult yet essential part of their work.

Methods & objectives
A cross sectional study was carried out in three central Hospitals: Omdurman teaching hospital, Khartoum north teaching hospital and Soba University hospital, Khartoum, Sudan from January 1st 2012 to February 28th 2012. A questionnaire was distributed, to determine how junior doctors cope with extended night calls by assessing three elements: mental readiness; physical readiness and Interaction with others and the system. The results were analyzed manually and using the SPSS.

Results
There was total sample coverage of 100 respondents. Seventy percent 70% were females and 30% were males doctors. Their ranking level in the medical profession is shown in Table 1. Sixty nine percent of the study population did not receive any orientation on how to survive and recover from the night calls. Among the 31% who were oriented, 60% received the orientation in hospitals, 20% in the Sudanese medical specialization board council and 20% in other settings which were not specified.

Table 1 Characteristics and background of study population

<table>
<thead>
<tr>
<th>Job rank</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>House officer</td>
<td>15</td>
<td>40</td>
</tr>
<tr>
<td>Medical officer</td>
<td>10</td>
<td>18</td>
</tr>
<tr>
<td>Registrar</td>
<td>5</td>
<td>12</td>
</tr>
</tbody>
</table>

Physical readiness of the participants for call nights is shown in Table 2. Only 5% of them slept well the night before their call. Wearing comfortable clothes and shoes all the time was reported by 46% and 50% respectively. Eating and drinking properly during the call night was practiced sometimes by 57% and all the time by 17%. As for the sleeping habits during call
nights, 49% sometimes took short naps during free time on a call night. After finishing the call only 42% went to sleep immediately. Only 19% of the study subjects never took caffeine containing food and drinks during a call night, as opposed to 30% who did.

Table 2 Physical readiness of junior doctors for night calls. (n=)

<table>
<thead>
<tr>
<th></th>
<th>All the time</th>
<th>Most of the time</th>
<th>Sometime</th>
<th>Never</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleeping well before</td>
<td>5</td>
<td>18</td>
<td>51</td>
<td>26</td>
</tr>
<tr>
<td>Wearing comfortable shoes</td>
<td>50</td>
<td>26</td>
<td>17</td>
<td>7</td>
</tr>
<tr>
<td>Wearing comfortable clothing</td>
<td>44</td>
<td>28</td>
<td>22</td>
<td>4</td>
</tr>
<tr>
<td>Eating and drinking properly</td>
<td>17</td>
<td>9</td>
<td>57</td>
<td>17</td>
</tr>
<tr>
<td>Taking a nap</td>
<td>9</td>
<td>21</td>
<td>49</td>
<td>21</td>
</tr>
<tr>
<td>Sleeping immediately after the call</td>
<td>27</td>
<td>42</td>
<td>14</td>
<td>17</td>
</tr>
</tbody>
</table>

Forty one percent of the study subjects kept a source of medical information during call nights all the time, 19% most of the time, 31% sometimes and 7% never kept it. Hand book was utilized by 61% as a major source of information, 11% use smart phone and 22% depended on asking their colleagues. One third kept a complete set of medical instruments during call nights all the time and another third kept it sometimes while 18% never did.

Punctuality was reported by 53% all the time; 33% most of the time; with 4% never arrived in time. A Cell phone was the dominant method of communication, it was used by 90% of the doctors. Calling a senior resident for help was reported by 70% all the time, by 17% most of the time and 13 % sometimes.

Receiving proper sign out (hand over) was claimed by 23%. On the other hand 40% believed that they gave detailed sign out to the others. Twelve percent did their sign out in person and 10% never practiced sign out Figure 1.

Figure 1 The attitude of junior doctors and others towards signing out

The reported overall level of preparedness, survival and recovery from call nights is shown in Figure 2. It seemed that less than 50% were ready, surviving and recovering from the night call.

Figure 2 Level of preparedness, survival and recovery from night calls among junior doctors
Discussion

Many studies were carried out across the world to validate the huge negative impact night shifts might have on the junior doctors regarding their performance, safety and learning abilities (5). The risk does not effect the mental, physical and emotional health of our junior doctors but extends to their patients as well. Looking at the back ground of our study subjects, 70% of our respondents were female doctors. It is noted in some medical schools in Sudan the ratio of females to males is 2:1. The implications of this need further assessment and longitudinal follow-up. We do not have objective data regarding the effect of gender on service duration, quality and accountability to the society need in Sudan.

Most of our study subjects (69%) have not received any orientation about readiness for the night calls. This calls requires a structured program either in the medical school or immediately before starting the job.

The poor sleeping habit of our study subjects was striking. Only 5% of them slept well before a call night. It has been consistent from previous studies that a steady sleeping routine, taking short nap (20 to 45 minutes) during a call night and a good sleeping hygiene are the most helpful for a successful call night (6). Hillson reported in a retrospective review that admissions after midnight were “associated with the highest rates of mortality whereas daytime admissions had the lowest rate of mortality. This was related to interns sleep deprivation and lack of supervision (7). Despite the difficulty encountered on the call night it was estimated that 70%-95% of residents did cope effectively well without emotional and behavioral impairment (8).

There was a wide variation on the ways the junior doctors made themselves comfortable and ready for long working hours. 81% of our junior doctors reached out for caffeine containing food and drinks during call nights with variable dependence and only 19% never used caffeine during night call. The on call doctor might need to balance the alertness gained by caffeine with its effect on recovery (9).

It is of utmost importance to have an access to an updated complete source of medical knowledge to reach for during a working night. Almost two thirds of the participants (60%) reported that they use a hand books as a major source of information. Allan et al reported that residents had many questions during clinical practice. Preceptors were used more commonly than all other resources combined and were the most dependable resource for residents to obtain answers (10). It is reassuring to find that most of our juniors (70%) reach out for help. One fifth of participants used smart phones. Internet is a useful and easily accessible source for information. This has to be balanced against the reliability, accuracy and ability to upraise the information. Krause et al reported that emergency medicine residents’ ability to answer clinic questions correctly by using Web sites from Google searches was poor. He claimed that the Internet appears to have given the residents a false sense of security in their answers (11). Rhebergen found that health care workers are often unable to find correct answers and misjudge the quality of the information they find when using web based common information sources (12). It will be helpful if our facilities can provide access to updated source of medical knowledge.

A well functioning team is crucial for successful night calls. To ensure efficiency of a team it is imperative to have a strong system of communication between junior doctors and the working staff. Two thirds (66%) of our study subjects had a good mean of communication with staff all the time during a night call with almost 90% of them using cell phones as a primary means of communication. Limitations of cell phones have to be considered and a backup plan is needed to overcome troubleshooting.

Conclusion

One half of the surveyed doctors had only fair to poor levels of preparedness, tolerated and recovery from night calls. A clear communication plan needs to be determined. Hospitals should consider a formal orientation of the new doctors and avail an easy access for medical information.

References


Case Report

Low grade penile epithelioid hemangioendothelioma in a one month old child
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*Al-Neelain University, **Gezira University

Abstract
Epithelioid hemangioendothelioma is a unique tumor of adult life which is characterized by an “epithelioid” or “histioctoid” endothelial cell. Epithelioid hemangioendothelioma of the penis is a rare but established entity. We report here a case of penile low-grade Epithelioid hemangioendothelioma in a one-month-old child who presented with distal penile swelling since birth. The diagnosis was confirmed by incisional biopsy.

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Case report
A one-month-old child was brought to the Khartoum Teaching Hospital with swelling at the tip of the penis since birth, which was increasing in size gradually and associated with burning micturition; it easily bled on touch. Two weeks later, it was infected with pussy discharge. On physical examination, the child general condition was good and his weight was 4 kg. He was afebrile with normal vital signs.

Locally there was a fungating 6 by 8 cm mass at the distal part of the penis. It was destroying the glans with irregular edges and it bled easily on touch and had blackish crust (figures 1&2).

Figure 1: ventral view of the penis

The CVS, respiratory system, CNS and limbs were normal. Investigations revealed Hb of 10gm/dl, TWBC 11000/dl, PLT 389,000/dl, blood urea 19mg/dl, creatinine 0.4 gm/dl, sodium 135 mmol/l and potassium 4.6 mmol/l. Abdomenal U/S was normal.

Incisional biopsy taken from the glandular swelling including part from the normal penile skin. The histopathology report showed a vascular tumor composed of endothelial cells within blood vessels as seen in reticulin in stained sections. The blood vessel wall marker CD34 was positive. The cells were polygonal with dark nuclei and scanty cytoplasm. The cells were negative for the epithelial Cell Marker CD EMA, which excludes an epithelial origin. They were also negative for the Leukocytes common Antigen LCA, which excludes a lymphoma. There were scattered mitosis and there was involvement of...
one of the resected margin. The diagnosis was low-grade hemangioendothelioma. The plan was to do amputation and reconstruction of the penis.

Discussion

Epithelioid vascular tumors are uncommon vascular neoplasms of uncertain pathogenesis, and they have a wide spectrum of biologic behavior. These tumors are a subtype of mesenchymal tumors, defined by their epithelioid morphology, which differentiates them from other vascular tumors. The spectrum of the epithelioid vascular tumors has been classified using histological descriptions in an attempt to predict their biological behavior: from the benign epithelioid hemangioma, to epithelioid hemangioendothelioma, and to the aggressive epithelioid angiosarcoma.\(^{(2)}\)

Epithelioid hemangioma is composed of well-formed vascular channels of epithelioid cells in a nodular architecture, with infiltrating lymphocytes and eosinophils.\(^{(3)}\) The lack of malignant histological features, such as necrosis, mitotic activity or nuclear atypia, distinguishes epithelioid hemangioma from the more-aggressive lesions within this diagnostic spectrum. The most frequent locations for epithelioid hemangioma are the head and extremities, with the penis a less common site of this disease.\(^{(3)}\) Penile epithelioid hemangioma most commonly consists of solitary, tender masses involving the dorsum of the penis, and occurs in men of a wide age range (23–75 years).\(^{(3)}\)

Angiosarcomas mark the most aggressive end of the epithelioid vascular tumor spectrum. These tumors have predominantly solid growth, nuclear pleomorphism, substantial mitotic figures, necrosis, and destructive growth, which gives epithelioid angiosarcoma a pseudogranulomatous appearance.\(^{(3,4,5)}\) Epithelioid angiosarcoma was first characterized by Enzinger\(^{(6)}\) in 1970, and these tumors most frequently occur at the head and neck (52% of lesions). The penis is a rare site of epithelioid angiosarcoma, with fewer than 20 cases reported.\(^{(4,5)}\) Approximately half these cases presented with symptoms of Peyronie disease, and the patients were usually younger than 40 years.\(^{(4,7)}\) The clinical course of epithelioid angiosarcoma is aggressive, with high rates of local recurrence (85%)\(^{(4,7)}\) and distant metastasis (20–50%).\(^{(4,7,8)}\) Median overall survival for patients with epithelioid angiosarcoma is 2.6 years, with a 5-year survival rate approaching 31%.\(^{(9)}\)

The reported patient was diagnosed with epithelioid hemangioendothelioma; this subtype of epithelioid vascular tumor lies between the extremes of epithelioid hemangioma and epithelioid angiosarcoma on the biological aggressiveness spectrum. Epithelioid hemangioendothelioma is characterized histologically as isolated nests of epithelioid endothelial cells within a hyaline matrix, but lacks the nuclear pleomorphism and mitotic activity seen in epithelioid angiosarcoma.\(^{(1,3,10)}\) Epithelioid hemangioendothelioma was first described by Weiss and Enzinger\(^{(1)}\) in 1982, and most commonly arises as multifocal disease in solid organs, bone, and deep soft tissue, with rarer presentations localized to the skin. Epithelioid hemangioendotheliomas were originally considered to be low-grade malignant lesions; however, they have now been upgraded to fully malignant in the 2002 WHO classification guidelines.\(^{(11)}\) These tumors have an overall local recurrence rate of 10%, a metastasis rate of 20–30%, and a mortality rate of 15%, although patients with epithelioid hemangioendothelioma have a better prognosis than patients with epithelioid angiosarcoma.\(^{(1,3,8,10)}\) Epithelioid hemangioendothelioma of the penis is a rare but established entity. To date, 18 cases of penile epithelioid hemangioendothelioma have been reported in the literature.\(^{(12,13,14,15)}\) Of these cases, two presented with metastasis and two with multifocal penile epithelioid hemangioendothelioma lesions;\(^{(12,15)}\) the patient presented in this article represents the first documented case in a newborn baby with penile low grade epithelioid hemangioendothelioma. Adult patients tend to be symptomatic with painful erections; the differential diagnosis for epithelioid hemangioendothelioma includes priapism, Peyronie disease, or superficial penile vein thrombosis.\(^{(15)}\)

Across the literature, a dichotomy exists for the biological behavior of epithelioid hemangioendothelioma. While simple excision has often been reported to result in cure, other authors quote recurrence rates of up to 40%, with 20–30% of patients progressing to metastatic disease.\(^{(13)}\) In an article published in 2008, Deyrup et al.\(^{(8)}\) proposed stratifying epithelioid hemangioendothelioma as low risk or high risk, on the basis of clinicopathological features.\(^{(8)}\) In their
article, multivariate analysis showed that increased mitotic activity (hazard ratio 10.03) and tumor size larger than 3.0 cm (hazard ratio 2.26) were associated with significantly decreased 5-year disease-specific survival compared with patients without these high-risk features (59% versus 100%). Nevertheless, low-risk cases still had metastasis rates of 15%, compared with a rate of 32% for high-risk cases. Both these rates are classified as malignant by the WHO. The current patient had aggressive clinical features, and mild pathological features including necrosis and a low mitotic rate; therefore, his tumor can be classified as low risk epithelioid hemangioendothelioma.

Treatment
As epithelioid vascular tumors are biologically heterogeneous, with no clear association between histological features and clinical course, prognostication of treatment outcome is difficult. Whereas surgical excision alone has proven curative in the management of penile epithelioid hemangioma, the fulminant course of epithelioid angiosarcoma requires wide local excision, lymph node dissection, and optional adjuvant therapy for solitary lesions to reduce the high rates of recurrence. Negative microscopic margins and superficial depth of invasion have both been correlated with significantly longer survival; however, response to treatment in these patients is typically poor.

Chemotherapy is traditionally reserved for locally advanced and metastatic tumors, and has never been investigated in the adjuvant setting. Case reports have documented various chemotherapeutic regimens with partial responses. To date, doxorubicin hydrochloride-based regimens have yielded the best overall response rates, with a progression-free survival of 3.7–5.4 months, and anecdotal reports have indicated full responses of angiosarcoma to liposomal doxorubicin hydrochloride.

Epithelioid hemangioendothelioma presents a management dilemma, as its clinical course encompasses a wide spectrum of biological potential between epithelioid hemangioma and epithelioid angiosarcoma. In case reports of patients with penile epithelioid hemangioendothelioma with low-risk features, some authors reported good results with local excision alone. These reports include cases of multifocal, synchronous epithelioid hemangioendothelioma lesions and those with multifocal recurrences of epithelioid hemangioendothelioma requiring repeat excisions, with no eventual tumor recurrences or metastases in the long term. In the current patient, the presence of localized lesion with low risk disease favoured complete local excision. Some authors have advocated adjuvant therapy to reduce metastatic potential and recurrence, especially for lesions with high-risk features. In one case report, which included a review of the literature, adjuvant radiation therapy to the primary lesion was shown to result in a disease-specific mortality rate of 50% at 1 year, with the other 50% of patients remaining clinically free of disease. Another patient with penile epithelioid hemangioendothelioma that had metastasized to the regional lymph nodes received adjuvant interferon α2b after surgical excision, and had no evidence of recurrence at 65 months. Multiple case reports of adjuvant chemotherapy have described partial responses to numerous agents before eventual cancer progression.

The current patient is planned for amputation and reconstruction of the penis because it was destroyed by the tumour.

Owing to the wide spectrum of biological behavior of epithelioid hemangioendothelioma, treatment should be tailored to the individual patient. The future management of epithelioid hemangioendothelioma is likely to be determined by the ongoing distinctions in histological features of low-risk and high-risk pathological subclassifications. Low-risk lesions will probably require only surgical excision, such as is required for epithelioid hemangioma, and high-risk lesions will probably require a multimodal approach, similar to the more-aggressive epithelioid angiosarcoma.

Conclusions
This case highlights the spectrum of clinical behavior of penile epithelioid hemangioendothelioma. In order to guide treatment, ongoing pathological distinctions are needed to characterize this type of tumor further.

However, the parents decided to take the baby patient abroad for treatment, taking with them the histopathology slide which was previously seen and
confirmed by Professor A.M. Elhassan. Therefore no photo of the histopathology is available.

References


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