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In adolescence, menstrual disturbances are commonly encountered. More than two third of adolescent problems are related to menstruation, amongst girls. The commonest menstrual disorders observed in this age group are: dysmenorrhoea (painful menstruation) amenorrhoea or oligomenorrhoea (absent or reduced menstruation). Dysfunctional uterine bleeding (DUB), menorrhagia (excessive and/or regular menstruation).
Neeta Trehan, Anusuya Gehlot, Kamal Khichi, Monika Sharma, Poonam Jakhar, Sahdev Choudhary

Review Article
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58 Update on Non-specific Leucorrhoea and its Management
The term leucorrhoea or “vaginal whites” is applied to cases of abnormal vaginal discharge, non-haemorrhagic in nature, which is not caused by neoplasm or other serious organic disease. Leucorrhoea is one of the three most common complaints in obstetric and medical practice the other two being pain and haemorrhage. Women suffering from leucorrhoea experience psychological disturbance and matrimonial disharmony.
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68 Developmental Language Disorder

The diagnosis of ‘developmental language disorder’ or ‘specific language impairment’ (SLI), previously known as developmental dysphasia, is applied when speech and language skills fall below nonverbal intelligence for no obvious reason; sensory impairment, gross neurological abnormality and pervasive developmental disorder, for example, are exclusionary criteria. Diagnosis usually involves a multidisciplinary assessment.

Kate Nation
Rates of live birth with assisted reproductive technology have usually been reported per cycle, but for women undergoing continuous treatment, cumulative live-birth rates are more relevant. A national US database has been used to estimate cumulative rates.

Data were available for 246,740 women (471,208 cycles, 140,859 live births). Live-birth rates decreased with increasing maternal age and increasing cycle number with autologous, but not with donor, oocytes. Conservative and optimal estimates of live-birth rates by the third cycle with autologous oocytes were 63.3% and 74.6% for women < 31 years old, 18.6% and 27.8% at ages 41 and 42, and 6.6% and 11.3% at age 43 or older. Using donor oocytes, the corresponding figures were 60% and 80% at all ages. Rates were higher with blastocyst embryos (transfer at day 5 or 6) than with cleavage embryos (day 2 or 3).

Live-birth rates similar to natural fecundity can be achieved with favourable maternal and embryo characteristics. The use of donor oocytes eliminates the decline in live-birth rates with age seen when autologous oocytes are used.


Urinary protein-to-creatinine or albumin-to-creatinine ratio to detect significant proteinuria in pregnancy

A systematic review and meta-analysis has addressed the use of spot urine protein-to-creatinine or albumin-to-creatinine ratio to detect significant proteinuria in pregnancy in the diagnosis of pre-eclampsia.

The analysis included 20 studies (2,978 women). Threshold values for protein-to-creatinine ratio ranged from 0.13 to 0.5 with sensitivity values between 0.65 and 0.89 and specificity of 0.63 to 0.87 for the detection of 24-hour urinary protein > 0.3 g/day. The optimum threshold values for protein-to-creatinine ratio appeared to be 0.30–0.35. There was insufficient evidence about the use of albumin-to-creatinine ratio. One study suggested that a value of > 2 mg/mmol was associated with a sensitivity and a specificity both of 0.94. There is insufficient evidence about the use of either test to predict adverse pregnancy outcome.

Urinary protein-to-creatinine ratio may be useful in the diagnosis of pre-eclampsia, but there is insufficient evidence about the use of albumin-to-creatinine ratio for this purpose or about the use of either test to predict adverse pregnancy outcome.

Morris RK et al. Diagnostic accuracy of spot urinary protein and albumin to creatinine ratios for detection of significant proteinuria or adverse pregnancy outcome in patients with suspected pre-eclampsia: systematic review and meta-analysis. BMJ 2012; 344: (July 21): 14 (e4342)

Reducing measles mortality

One global goal was to halve measles deaths between 1999 and 2005, and that was achieved. A new goal was then set to reduce measles mortality by 90% between 2000 and 2010. There has been no endemic measles virus transmission in the Americas since 2002, and only the southeast Asia region of the World Health Organization has not set an aim of measles elimination by 2020. Measles mortality fell by an estimated 74% between 2000 and 2010, from 535,300 to 139,300 deaths. All regions except southeast Asia achieved a reduction of > 75%. In India, measles deaths fell by 25% from 88,000 to 65,500. In 2010, almost half (47%) of all deaths from measles were in India and 56% were in Africa. Achievement of the 2000–2010 goal was impeded by delayed implementation of disease control in India and outbreaks of measles in Africa. Greater political and financial commitment are needed.

The diagnosis of asthma is made on the basis of typical symptoms and abnormalities in lung function. The key clinical features of asthma include the following.

**Variable Airways Obstruction**

Airways obstruction in asthma, as measured by spirometry, may vary spontaneously from none to severe in the course of hours to minutes and improves after suitable therapy. Obstruction, particularly of the smaller airways, in asthmatics causes shortness of breath, impaired exercise tolerance, tightness in the chest which may be perceived as wheeze and chest hyperinflation (small airways obstruction prevents complete emptying of the alveoli, causing gas trapping).

**Non-specific Bronchial Hyper-reactivity**

This refers to the tendency of asthmatic airways to constrict in response to a whole host of non-specific (that is, non-immunological) stimuli (including, for example, strong smells, cold air, fog, smoke, exercise, aerosol sprays, dust) that would not cause clinically significant bronchoconstriction in non-asthmatics. Bronchial hyper-reactivity causes excessive cough and contributes to bronchospasm, which may have different triggers in different patients.

**HISTOPATHOLOGY**

Asthma is characterized by inflammatory changes throughout the airways, but not the
alveoli or lung parenchyma. The inflammation is characterized by the activation of CD4+ helper T lymphocytes, as well as a selective accumulation of eosinophil leukocytes in the bronchial mucosa (Figures 1 and 2), although these changes do not allow a definitive diagnosis on histopathological grounds. Some chronic, severe asthmatics show a paucity of mucosal eosinophils but a more prominent neutrophil leukocyte infiltrate. Mast cells are present in the bronchial mucosa, as they are at all mucosal surfaces, but their numbers are not particularly elevated in asthmatics. It has so far not been possible to associate aetiological subdivisions of asthma with reproducible and discernible variability in histopathology.

Asthma is also associated with structural changes in the airways collectively termed ‘airways remodelling’ (Figure 3). These include hypertrophy and hyperplasia of airways smooth muscle cells, increased numbers of mucous goblet cells in the airways epithelium, laying down of fibrous proteins (including collagen, fibronectin and tenascin) beneath the epithelial basement membrane and in the submucosa, and neovascularization (proliferation of vascular capillary beds within the submucosa).

**PATHOPHYSIOLOGY**

Asthmatic inflammation appears to be coordinated principally by activated CD4+ T lymphocytes of the Th2 type phenotype, characterized particularly by the production of the cytokines interleukin (IL)-4, IL-13 and IL-5 (Figure 2). The cytokine IL-5 acts on eosinophils, while IL-4 and IL-13 up-regulate adhesion molecules in the capillary endothelium of the bronchial mucosa, resulting in increased adhesion of eosinophils to the endothelium whereby they are recruited into the tissues. Once in the tissues, IL-5 prolongs the survival of eosinophils and activates the release of their granule proteins. These proteins carry a high negative charge and are cytotoxic. Mucosal epithelial damage is thought to be one cause of hyper-responsive airways in asthma, although the precise mechanism is unknown. Other eosinophil mediators, such as cysteinyl leukotrienes, promote vascular leakage—and thus oedema of the lining of the airways—and are also very potent constrictors of bronchial smooth muscle. All of these effects probably contribute to airways obstruction.

These same cytokines, as well as tumour necrosis factor (TNF)-alpha, have been implicated in causing remodelling changes in the airways as described above. Some cytokines, such as IL-13, act directly on target cells, such as mucous glands, while others act through intermediary cells, such as eosinophils. For example, activated eosinophils produce a growth factor called transforming growth factor (TGF)-beta which acts on fibroblasts, causing them to transform into myofibroblasts, a cross between fibroblasts and smooth muscle cells which are responsible for the laying down of fibrous proteins in the bronchial mucosa. TGF-beta and other growth-regulating cytokines also cause increased proliferation of airways smooth muscle cells. Injured epithelial cells also release TGF-beta,
forming the so-called ‘epithelial mesenchymal trophic unit’, which may also contribute to remodelling changes in asthmatic airways.  

Finally, IL-4 and IL-13 are the only human cytokines which induce B lymphocytes to switch to IgE synthesis following activation by interaction with antigen-specific T cells. (Figure 2) These cytokines are, therefore, implicated in the pathogenesis of atopy (a propensity for inappropriate production of IgE antibodies against antigens or ‘allergens’ encountered at mucosal surfaces detected by skin prick or laboratory tests).

Cytokines derived largely from T cells are thought to drive most of the inflammatory and airways structural changes characteristic of asthma, regardless of its aetiology, and also play an important role in the development of atopy. (Figure 4) Airways structural cells, as well as other infiltrating leukocytes, including eosinophils and mast cells, are likely to also contribute to the production of cytokines and growth factors causing airways remodelling.

The antigenic drive to T cell activation in asthma is unknown. There is a tacit assumption that inflammation in asthma is driven largely by T cells which recognize inhaled allergens, some of which may also interact with allergen-specific B cells resulting in IgE production and the atopic phenotype. All individuals, however, have allergen-specific
T cells, and a major facet of current research in asthma and atopy is to attempt to understand why allergens produce a particularly exuberant Th2-type T cell response in patients with asthma and atopy, leading to inflammation of the bronchial mucosa and the atopic phenotype on the one hand, with inappropriate production of IgE against allergens on the other. It is quite possible that other antigens, such as viral antigens, also drive T cell activation in asthma in particular circumstances. T cell activation may become self-perpetuating with time in the manner of an autoimmune disease.

GAPS IN OUR KNOWLEDGE

It is easy to envisage broadly how inflammation, leading to oedema of the bronchial mucosa caused by capillary proliferation and leakage; hyperplasia of mucus glands with the production of sticky mucus plugs; and bronchial smooth muscle hyperplasia and excitability may result in the airways narrowing that characterizes asthma. There is strong circumstantial evidence to suggest that bronchial inflammation is responsible for the symptoms of asthma, since all asthmatics show it, and it is reduced by successful treatment along with reduction in clinical symptoms. The precise mechanistic links between the inflammatory process and the generation of symptoms, variable airways obstruction and bronchial hyper-responsiveness in asthma are, however, very poorly characterized. There is very little information as to if and how these inflammatory changes regulate short-term variability in the severity of asthma or responses to non-specific exacerbating factors for asthma, such as exercise, cold air, fog and smoke. While airways obstruction is characteristically reversible in asthma, some asthmatics develop a degree of irreversible airways obstruction which is thought to be caused by remodelling changes, although again precisely how these changes cause irreversible airways obstruction is not clear.4,5,8

INFLAMMATION AND ASTHMA THERAPY

Corticosteroids strongly inhibit T cell activation and cytokine production,1 and this is thought to be one principal mechanism whereby they ameliorate asthma. It has been shown that corticosteroid therapy of asthmatics reduces the expression of T cell-derived cytokines in the bronchial mucosa, and this in turn results in reduced infiltration of inflammatory cells, such as eosinophils. In contrast, corticosteroids have few direct inhibitory effects on granulocytes, such as eosinophils and neutrophils, and may not reverse all remodelling changes. Other actions of corticosteroids, such as their reduction of vascular leakiness, may also be relevant in reducing mucosal oedema and thereby improving airways obstruction and bronchial hyper-responsiveness.

Cysteinyl leukotrienes are important pro-inflammatory products of cells implicated in asthma, particularly eosinophils.6 They have many effects which may be relevant to asthma pathophysiology, causing capillary leakage, bronchoconstriction and further eosinophil recruitment. Cysteinyl leukotriene receptor blockers have a proven role in the treatment of some, but not all, asthmatics.

Beta-2 adrenoreceptor agonists relax bronchial smooth muscle and are useful as ‘reliever’ therapy for acute symptoms of asthma. They have not been shown convincingly to exert an anti-inflammatory effect in asthma, although there is some evidence that long-acting beta-agonists may enhance some of the anti-inflammatory effects of corticosteroids.
AETIOLOGY OF ASTHMA

Genetic Susceptibility
The risk of developing asthma tends to run in families. Twin studies estimate the proportion of asthma risk to be 50–60% genetically determined, although, as with many diseases, there are likely extensive and complex interactions of gene effects with environmental influences. Genome screens have linked inheritance of various chromosomal regions with an increased risk of asthma. Some of these regions contain genes encoding cytokines, such as IL-4 or IL-13, or their receptors, implicated in asthma pathogenesis, suggesting that genetic variability in the expression or actions of these mediators may contribute to asthma risk. More recent positional cloning strategies have identified new genes, such as ADAM33, the products of which do not play a role in known asthma pathways but are involved in the normal development of the airways during embryogenesis, raising the fascinating possibility that variability, as yet uncharacterized, in the structure or development of the airways predisposes some individuals to asthma.

Role of Allergen Exposure
When atopic patients inhale allergens to which they are clinically sensitized through the production of allergen-specific IgE, this cross-links surface-bound IgE on mast cells within the respiratory mucosa, causing them to degranulate acutely and release their own series of inflammatory mediators, in particular histamine, prostaglandin D2, and leukotrienes. These mediators make asthma acutely worse since they all cause bronchial smooth muscle contraction, vascular leakage and inflammatory cell recruitment. Thus, allergen exposure is an important immunologically specific trigger in some, but not all, asthmatics, acting on the background of mucosal inflammation instigated by T cells. These patients may have other diseases associated with atopy (eczema and allergic rhinitis).

Early life sensitization to allergens, particularly indoor allergens, such as house dust mite, is a major risk factor for the development of asthma in children, but only in the genetically predisposed, raising doubts as to whether allergic sensitization is actually causative of asthma or reflects parallel susceptibility pathways arising from common genetic origins. Many atopic patients do not develop asthma. Furthermore, asthma developing later in life is less likely to be associated with atopy, suggesting that IgE sensitization to allergens is neither necessary nor sufficient for the development of asthma.

Occupational Asthma
Some individuals develop asthma for the first time after exposure to occupational agents, which may be broadly divided into reactive chemicals (such as isocyanates) or proteins (such as wheat flour). Proteins
activate T cells directly in the manner of an inhaled allergen and, like allergens, often induce an associated IgE response. Reactive chemicals react with native body proteins, such as albumin, creating new antigens which are recognized as ‘foreign’ by T cells. The pathophysiology of occupational asthma, once developed, appears to be indistinguishable from that seen in other clinical phenotypes of asthma. Again, it is not clear what governs individual susceptibility.

Other Influences on the Development of Asthma

Asthma and atopy are, geographically, diseases of developed countries. This has resulted in speculation about the role of ‘Westernized’ society in their causation.

Pollution and Smoking

Many pollutants exacerbate asthma, but there is little evidence that they predispose to its development. Air pollution has declined in many Western industrialized countries while asthma prevalence has increased. Epidemiological and experimental evidence suggests that diesel exhaust particulates and ozone promote sensitization to allergens. Exposure of children to tobacco smoke in utero or early childhood increases their risk of developing wheeze. Smoking in adults increases the risk of developing asthma, including occupational asthma. The pathophysiological mechanisms are unknown.

Diet

The growth of the fast food diet and escalating obesity have led to speculation about lack of nutrients (antioxidant vitamins, omega-3 fatty acids, selenium, magnesium, sodium and zinc) and obesity playing a role in asthma causation, but there is no conclusive evidence. Breastfeeding reduces the risk of eczema in atopic ‘at risk’ children, but the evidence relating to asthma is inconclusive.

Infection

The pattern of microbial exposure in infancy and childhood has changed as a result of a cleaner environment and widespread use of antibiotics and vaccination. The ‘hygiene hypothesis’ invokes this as a risk factor for asthma and atopy. The precise mechanisms are unknown, but the hypothesis has focused research on the effects of alteration of the intestinal flora early in life, exposure to airborne bacterial products (such as endotoxins on farms) and the influence of specific (viral, helminthic) infections on the risk of developing asthma. Research is ongoing.


About the Author

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REFERENCES

Case of the Month

Woman at 24 Weeks of Gestational Age with Abdominal Pain and Loss of Foetal Movement

Varsha Desmukh, VY Kalyankar, Kanan Yelikar, PS Deshmukh, SM Rijhwani

Case Report

A 20 years old female, primigravida was referred to emergency by general practitioner at 24 weeks of gestational age history of abdominal pain since 1 week and loss of foetal movements since 2 days. There was no history of discharge per vaginum, abdominal trauma or any bowel or bladder disturbances. Her medical and surgical history was uneventful. Her present pregnancy was unremarkable till now. She had no investigations done and had not attended any antenatal clinic.

On admission, her general condition was good. Pulse rate was 88/min; blood pressure was 110/70 mmHg. There was a mass arising from pelvis corresponding to 24 weeks of pregnancy. Surface was smooth, non mobile. Per speculum examination did not reveal any vaginal or cervical pathology. Cervix was long, firm and posterior. Os was closed. There was no adnexal mass felt. No evidence of bleeding per vaginum. A clinical impression of threatened preterm labour was made.

Transabdominal ultrasound was done immediately and the findings were as follows: single intrauterine pregnancy with no foetal cardiac activity, reduced liquor volume with amniotic fluid index (AFI) of 2.5 cm at gestational age of 25.4 weeks. Her haemoglobin was 11.2 gm%, platelet count was 320*10^9/L and coagulation profile was within normal limits. Blood group was B positive. Clinical diagnosis was intrauterine foetal demise at 25.4 weeks of gestational age with unfavourable cervix.

Labour was induced with 200 microgram of misoprostol in posterior vaginal fornix every 6 hours apart for a total of 4 doses. This was however unsuccessful on two different occasions 72 hours apart. There was no complication associated with attempts of induction of labour. The os was closed, uneffaced still unfavourable. Based on two unsuccessful attempts at induction of labour, extraterine pregnancy was suspected. A repeat scan was done which could not give any clue regarding extraterine pregnancy or rudimentary horn. MRI was done which showed undeveloped horn in left lateral position (Figure 1). Both kidneys found to be normal.

(Continued on page 64)
INTRODUCTION

Pre-eclampsia and eclampsia are unpredictable multi-organ disorders unique to human pregnancy. Eclampsia complicating human pregnancy is common and forms one of the deadly triad, along with haemorrhage and infection. It is associated with significant maternal and neonatal morbidity and mortality worldwide.

Its incidence is 1 in 500 to 1 in 30 pregnancies in India. It is estimated that in developing countries 10% of all maternal death are associated with eclampsia. Complications responsible for most maternal death include cerebrovascular accident (haemorrhage, thrombosis) pulmonary oedema, cardiac arrest, and renal, hepatic and respiratory failure. Conde-Angudelo and Kafury-Goeta divided eclampsia into uncomplicated and complicated. They defined complicated eclampsia as eclampsia complicated by intracerebral haemorrhage, pulmonary oedema, disseminated intravascular coagulation, abruption placentae, HELLP syndrome, pulmonary aspiration, renal, hepatic or respiratory failure.

Research in understanding of pathophysiology of eclampsia, popularisation of magnesium sulphate regimen for convulsion control and opening of field of critical care in obstetrics has made this classification possible. The patient with eclampsia converting into complicated eclampsia is stopped by keen observation and timely intervention.
to halt pathogenetic process. This would lead to decrease in multi-system complication, maternal morbidity and mortality.

Purpose of this study was to accessed the incidence of complicated eclampsia, maternal and perinatal mortality associated with it and to know the socio-economic profile of eclampsia patient.

MATERIAL AND METHODS

From May 2006 to December 2006, 100 consecutive eclampsia patient treated prospectively in Government Medical College and Guru Govind Singhji Memorial Hospital Nanded were analysed. It is a district hospital where patients are referred from places in approximately 100 Km radiuses. It serves urban as well as rural population. Most patients belong to low and low-mid socio-economic class. Clinical and laboratory data of 100-eclampsia patient was analysed to know the incidence of complicated eclampsia and the nature of complications.

Eclampsia cases for inclusion in this study were defined as seizures occurring antepartum after completing 20 weeks of pregnancy, intrapartum, postpartum in the presence of clinical features of pre-eclampsia that cannot be attributed to other causes. Complicated case of eclampsia was defined as eclampsia complicated by intracerebral haemorrhage, pulmonary oedema, disseminated intravascular coagulation, abruption placenta, haemolysis, elevated liver enzymes, low platelet (HELLP) syndrome, pulmonary aspiration or renal, hepatic or respiratory failures.

During the study period the management of eclampsia patient remained unchanged and it continued as per the protocol practiced earlier. All cases diagnosed to have eclampsia by the specialist on duty (lecturer) were included in the study. Cases where mark “?” was put, before diagnosis “eclampsia”, were not included.

All cases of eclampsia that developed complications listed in above definition any time after admission along with all those cases who were admitted with complications were included in the study. Total 100 consecutive admissions of eclampsia were included in this study.

Eclamptic women those coming from Gram Panchayat area were considered rural and those coming from Nagarpalika and Mahanagarpalika were considered as urban.

Combining clinical features and laboratory data did diagnosis of complicated eclampsia. Hb%, Blood group, Urine, Albumin, Sugar, Coagulation profile (Bleeding time, Clotting time), Liver function tests, Kidney function tests were available for all cases. Ophthalmic fundus examination, ultrasonography of abdomen was subject to availability of experts. Platelet count was available to all cases only during office hours and was therefore offered to cases, which continued to need it even after emergency hours. CT scan of brain was advised only in those cases where patients were comatose for more than 12 hours, and hospital regulations permitted. As per hospital rules, patient pay for cost of CT scan, if not belonging to “below poverty line” category. X-ray chest was advised for all those cases that had adventitious sounds on auscultation.

The maternal and perinatal mortality were analysed. Socio-economic status was assessed.

Statistician was involved in sample size calculation and data analysis. The incidence of eclampsia in India is 1 in 500 pregnancies to 1 in 30 pregnancies. At our institution it is 3 in 100 labour room admissions. This gives $p_1=0.20\%$, $p_2=3.33\%$, $p=3.00\%$. Therefore, $n=\frac{z^2pq}{(p_1-p_2)^2}$ i.e., $= \frac{4\times3\times97}{118} = 118$. So, $n$ for this study was decided as 100 (sample size). Statistical tests used in analysing data in this study are z-test, chi-sq test, t-test (for proportion, for incidence).
The study was carried over a period of 5 months. During this period, there were 3228 births. Incidence of eclampsia was found to be 30.97/1000 births. Fifteen women belonged to complicated eclampsia group giving an incidence of 4.64/1000 births. Incidence of uncomplicated eclampsia (85 cases) was 26.33/1000 birth. Table 1 shows distribution of cases according to type of eclampsia, and its relation to death and survival. There were no deaths in uncomplicated group, all the six deaths occurred in women having complications.

The residential status (urban/ rural), antenatal registration status, and the economic status (average income), did not differ in complicated and un-complicated groups (Table 2).

Out of 15 complicated cases, 9 cases had multi-organ affection, 6 died from this group. No woman died from group of six cases, which had only single

![Table 1. Eclampsia type, survival and death](image1)

<table>
<thead>
<tr>
<th>Complicated (n=15)</th>
<th>Uncomplicated (n=85)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ante-partum</td>
<td>Intra-partum</td>
<td>Post-partum</td>
</tr>
<tr>
<td>Survival</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Death</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>2</td>
</tr>
</tbody>
</table>

![Table 2. Social status of the patients included in the study](image2)

<table>
<thead>
<tr>
<th>Complicated</th>
<th>Uncomplicated</th>
<th>Total</th>
<th>Statistical tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rural (%)</td>
<td>14 (17.72%)</td>
<td>65 (82.27%)</td>
<td>79</td>
</tr>
<tr>
<td>Urban (%)</td>
<td>01 (4.76%)</td>
<td>20 (95.24%)</td>
<td>21</td>
</tr>
<tr>
<td>Unregistered cases (%)</td>
<td>12 (80.00)</td>
<td>55 (64.71)</td>
<td>67</td>
</tr>
<tr>
<td>Registered cases (%)</td>
<td>03 (20.00)</td>
<td>30 (30.29)</td>
<td>33</td>
</tr>
<tr>
<td>Average income in Rs. (Range) ± SD</td>
<td>Rs. 1253.33 (500 to 4000) ±  1315.73</td>
<td>Rs.1242.35 (100 to 10000) ±  923.40</td>
<td></td>
</tr>
</tbody>
</table>

![Table 3. Type of complication and survival](image3)

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Complications</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>05</td>
<td>ARF, HELLP syndrome</td>
<td>Survived</td>
</tr>
<tr>
<td>11</td>
<td>DIC, aspiration pneumonitis</td>
<td>Mortality</td>
</tr>
<tr>
<td>29</td>
<td>Pulmonary oedema, respiratory failure</td>
<td>Mortality</td>
</tr>
<tr>
<td>30</td>
<td>DIC, ARF, septicemic shock</td>
<td>Mortality</td>
</tr>
<tr>
<td>45</td>
<td>ARF, respiratory failure</td>
<td>Survived</td>
</tr>
<tr>
<td>61</td>
<td>HELLP syndrome, DIC hepatic failure</td>
<td>Mortality</td>
</tr>
<tr>
<td>64</td>
<td>ARDS, ARF, cerebral infarcts</td>
<td>Mortality</td>
</tr>
<tr>
<td>84</td>
<td>Respiratory failure, intracranial haemorrhage</td>
<td>Mortality</td>
</tr>
<tr>
<td>88</td>
<td>ARF, HELLP syndrome</td>
<td>Survived</td>
</tr>
<tr>
<td>50</td>
<td>HELLP syndrome</td>
<td>Survived</td>
</tr>
<tr>
<td>51</td>
<td>Pulmonary oedema</td>
<td>Survived</td>
</tr>
<tr>
<td>52</td>
<td>Pulmonary oedema</td>
<td>Survived</td>
</tr>
<tr>
<td>74</td>
<td>Abruptio Placenta</td>
<td>Survived</td>
</tr>
<tr>
<td>75</td>
<td>ARF</td>
<td>Survived</td>
</tr>
<tr>
<td>97</td>
<td>ARF</td>
<td>Survived</td>
</tr>
</tbody>
</table>
organ affection (Table 3). The commonest complication was renal failure (7 cases); next common was HELLP Syndrome (4 cases). The other complications were intracerebral haemorrhage (2 cases), disseminated intravascular coagulation (3 cases), cerebral oedema (3 cases), pulmonary complications were described in 7 instances (oedema 3 cases, aspiration 1 case, respiratory failure 3 cases), hepatic failure, placental abruption and atonic PPH in one case each. Many cases had more than one complication (Table 4). Perinatal mortality did not differ statistically in complicated and uncomplicated groups. Fifteen complicated cases had 8 perinatal losses, 85 uncomplicated cases had 26 perinatal losses (z-test; p>0.05, insignificant difference). Referral notes were analysed to know the treatment given by referring doctor (Table 5). These referring doctors used magnesium sulfate in very few cases; diazepam was commonly used.

**DISCUSSION**

Eclampsia is one of the most dreaded complications of pregnancy. Because of its sudden occurrence the patient’s relatives are apprehensive and are interested in knowing the prognosis. Treating doctor needs to give an answer that is supported by scientific data. In this regard, categorisation of eclampsia patients into complicated and uncomplicated is helpful. This categorisation can be explained to the patient’s relatives using obvious clinical data and laboratory reports. As complicated eclampsia has a definite risk of death, this categorisation also helps in decision of transferring patients to critical care.

### Table 4. Types of complications

<table>
<thead>
<tr>
<th>Complications</th>
<th>No. of Cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal failure</td>
<td>07</td>
<td>25</td>
</tr>
<tr>
<td>* HELLP syndrome</td>
<td>04</td>
<td>14.28</td>
</tr>
<tr>
<td>Pulmonary oedema</td>
<td>03</td>
<td>10.71</td>
</tr>
<tr>
<td>DIC</td>
<td>03</td>
<td>10.71</td>
</tr>
<tr>
<td>Cerebral oedema</td>
<td>03</td>
<td>10.71</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>03</td>
<td>10.71</td>
</tr>
<tr>
<td>Intracerebral haemorrhage</td>
<td>02</td>
<td>7.14</td>
</tr>
<tr>
<td>Abruptio placenta</td>
<td>01</td>
<td>3.57</td>
</tr>
<tr>
<td>Pulmonary aspiration</td>
<td>01</td>
<td>3.57</td>
</tr>
<tr>
<td>Hepatic failure</td>
<td>01</td>
<td>3.57</td>
</tr>
<tr>
<td>Atonic PPH</td>
<td>01</td>
<td>3.57</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>29</strong></td>
<td></td>
</tr>
</tbody>
</table>

Many cases had more than one complication hence the no. of cases is 28 instead of 15. *HELLP Syndrome includes partial as well as complete.

### Table 5. Drugs used at peripheral hospitals (n=29)

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Complicated</th>
<th>Patient (%)</th>
<th>Uncomplicated</th>
<th>Patient (%)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inj. MgSO4</td>
<td>3</td>
<td>20.00</td>
<td>8</td>
<td>9.41</td>
<td>11</td>
</tr>
<tr>
<td>Inj. Diazepam</td>
<td>2</td>
<td>13.33</td>
<td>18</td>
<td>21.17</td>
<td>20</td>
</tr>
<tr>
<td>Tab. Nifedipin</td>
<td>2</td>
<td>13.33</td>
<td>15</td>
<td>7.64</td>
<td>17</td>
</tr>
<tr>
<td>Inj. Mannitol</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1.17</td>
<td>1</td>
</tr>
<tr>
<td>Inj. Phenytoin Sodium</td>
<td>1</td>
<td>6.66</td>
<td>1</td>
<td>1.17</td>
<td>2</td>
</tr>
<tr>
<td>Inj. Frusemide</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1.17</td>
<td>1</td>
</tr>
<tr>
<td>Inj. Promethazine (phenargan)</td>
<td>1</td>
<td>6.66</td>
<td>2</td>
<td>2.35</td>
<td>3</td>
</tr>
<tr>
<td>Tab. Alpha methyl- dopa</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>2.35</td>
<td>2</td>
</tr>
</tbody>
</table>

Diazepam is more frequently used at periphery than magnesium sulphate.
units. After establishing diagnosis of eclampsia, which is often easy, the patient should be rapidly and thoroughly assessed for complications. For this clinical data, laboratory investigation and imaging techniques need to be used. This should become a standard practice in eclampsia management. In spite of worldwide proven success of magnesium sulphate in controlling eclampsia convulsions, peripheral healthcare practitioners are still seen to use other less effective drugs. Linking evidence-based medicine to the drug marketing-cum-doctor education might help rapid spread of right messages to the peripheral doctors.

CONCLUSION

Although eclampsia in itself is a complication of pregnancy, it needs to be categorised into complicated and uncomplicated depending upon the presence (complicated) or absence (uncomplicated) of organ/system dysfunction or failure. In this observational study, uncomplicated eclampsia group had no maternal mortality. Six deaths, from this study of 100 cases of eclampsia, belonged to complicated eclampsia group. All these 6 cases had more than one organ dysfunction; cases of complicated eclampsia having single organ dysfunction had no deaths. Thus, eclampsia cases having organ/system dysfunction should be transferred to and cared in critical care units, and should be made aware of possible bad outcome. Magnesium sulfate is yet unknown to many peripheral doctors.

About the Authors
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REFERENCES
INTRODUCTION

In adolescence, menstrual disturbances are commonly encountered. More than two third of adolescent problems are related to menstruation, amongst girls.

The commonest menstrual disorders observed in this age group are:

- Dysmenorrhea (painful menstruation)
- Amenorrhea or oligomenorrhea (absent or reduced menstruation)
- Dysfunctional uterine bleeding (DUB), menorrhagia (excessive and/or regular menstruation)

The hypothalamic pituitary gonadotrophin (HPG) system is the mediator of menstrual cycle. A failure of this system may lead to amenorrhea or sometimes variation in menstruation. Menstrual problems are common during adolescence due to slow maturation of the system and can last up to 2–5 years after menarche. They usually lack the positive feedback mechanism to induce luteinising hormone (LH) surge and subsequent ovulation, despite increased follicular oestrogen levels. Negative oestrogen feedback is intact as evidenced by suppression of FSH, LH and GnRH levels by high oestrogen. This indicates that pubertal anovulation is probably a hypothalamic malfunction rather than a pituitary one.¹

DYSMENORRHOEA

It is one of the common gynaecological complaints during adolescence. About 60% of the girls of 12–17 years of age group complain of dysmenorrhea. However, only 15% seek medical advice.

¹
First few periods are generally pain free due to anovulation. A heavy dragging pelvic pain is common than actual dysmenorrhea. This pain is due to the pelvic vascular engorgement under the effects of sex steroids. Dysmenorrhea may be primary or secondary.

**Primary Dysmenorrhea (spasmodic)**

Primary dysmenorrhea develops early after uterus menarche, within first 2 years. It is defined as painful menstrual cramps in the absence of any clinically detectable pelvic pathology. Possible diagnosis of the cause in atypical severe pain are endocrinal, myometrial disturbed action, prostaglandins and vasopressin.

It also observed that there is high intrauterine tone, elevated intrauterine active pressure, frequent uterine contractions as well as in coordinate myometrial action in these girls. Pain is usually described as crampy and lasts from a few hours to a couple of days. Girls who are overweight have twice the risk of having severe and prolonged cramping as compared to girls who are not overweight. Smokers also have 50% higher risk than non smokers. Girls who start menstruating at the age of 11 years or younger are at higher risk of severe pain and longer menstrual cycles.

**Secondary Dysmenorrhea (congestive)**

Secondary dysmenorrhea may occur many years after menarche. The pain is usually more severe and precedes periods by several days. Colicky pain before the flow and relieved with menstruation is the classic presentation. Common causes include endometriosis, pelvic inflammation disease (PID) and congenital genital tract malformations (bicornuate, subseptate uterus), cervical stenosis, transverse vaginal septum, fibroids, uterine polyps, adenomyosis, intrauterine adhesions, IUCD etc.

**Diagnosis**

Careful history is essential, including the emotional state of a girl. Pelvic examination is avoided. But sometimes, gentle one finger vaginal examination after good counselling may be required. One can diagnose major genital tract malformation, presence of recto vaginal nodule or pelvic masses, vaginal and pelvic infections with reasonable accuracy. Abdominal ultrasonography and rarely a diagnostic laparoscopy may be helpful in the diagnosis of the cause in atypical severe pain.

**Management**

Management includes detailed counselling as well as explanation about the pathophysiology of primary dysmenorrhea. It also includes:

- **Diet**: Salt restriction, reduced intake of caffeine, sugar and alcohol may be beneficial. Supplements of fish oil (omega-3 fatty acids) appeared to reduce heavy and painful bleeding in adolescent girls, as per a Danish study.

- **Exercise**: Exercise in moderation and back massage is helpful. Acupressure, stress reduction, yoga and meditation may be also beneficial in some cases.

- **Thermotherapy**: A continuous low of level topical heat provides great pain relief in the form of a heat wrap. Thermacare worn for 8 hours/day may provide pain relief for 24 hours.

- **Analgesics**: Painkiller like paracetamol are effective in cases of milder discomfort.

- **Anti-prostaglandin agents**: NSAIDs are the best and established in initial therapy for dysmenorrhea. These have a direct analgesic effect through the initiation of prostaglandin synthesis and also cause decrease in the menstrual blood flow. Frequently used NSAIDs are Ibuprofen, Diclofenac sodium, Naproxen, Indomethacin, Mefenamic acid and Flufenamic acid.
**Spasmolytics**: Spasmolytics like Drotaverine hydrochloride 80–240 mg/day gives excellent results.

**Inhibition of ovulation**: Oral contraception pills (OCPs), Progesterone only pill, Danazol etc.

**Laparoscopy**: Laparoscopy for endometriosis or PID is useful.

**Support of psychologist**: Psychologist’s help may be sought, if needed.

**AMENORRHOEA**

**Primary Amenorrhoea**
It is primary amenorrhoea, when a girl does not start menstruation by the age of 16 years or so. However, by the age of 14, if the girl has never menstruated, one needs to conduct a preliminary clinical check up and an ultrasonography to rule out major disorders like general endocrine disorders, cryptomenorrhoea, absence of uterus etc. Once reassured of absence of these, a more detailed check up is deferred upto 16 years. If absence of uterus is noted or if the ovarian follicles are not seen at laparoscopy and in case of streak gonads, an ovarian biopsy is indicated. Oestrogen replacement has to be given in these girls for a long time.

**Causes of Primary Amenorrhoea**

**CNS disorders**: They suppress hypothalamic activity. The common causes are chronic CNS disease, tumours (e.g., craniopharyngioma, glioma) as well as mass lesions such as glioma congenital lack of GnRH, anorexia nervosa, drugs (antihypertensives, chemotherapeutic drugs, antidepressants and narcotic drugs). CNS irradiation, stress etc.

**Pituitary disorders**: Hypopituitarism, tumours (prolactinoma), haemochromatosis etc.

**Thyroid dysfunction**: Hypothyroidism/hyperthyroidism.

**Adrenal dysfunction**: Congenital adrenal hyperplasia, tumour, Cushing syndrome etc.

**Ovarian**: Premature ovarian failure (POF), gonadal dysgenesis, PCOS, androgen producing tumours (arrhenoblastoma, theca cell tumour), etc.

**Outflow tract dysfunction**: Uterine agenesis, Asherman’s syndrome, cervical/vaginal agenesis, imperforate hymen etc.

**Pregnancy**: Pregnancy in sexually active teenage girls should be ruled out.

**Diagnosis**

**History**: Careful history to be taken regarding recent weight change, history of sexual activity, any use of medications etc is useful.

**General examination**: Look for height, virilisation, indifferent sex characters (Tanner staging and body habitus), secondary sex characters, thyroid swelling, galactorrhoea, obesity, exercise and emotional stress levels. Rule out the systemic causes associated with it.

**Gynaecological examination**: To be done if indicated.

**Investigations**: Depending upon the cause, investigations may be done as follows:

- CBC
- Thyroid profile, serum prolactin
- Ultrasonography scan abdominal/transvaginal ultrasonography
- Laparoscopy/hysteroscopy

**Management**

Sympathy and politeness are necessary to ease the anxiety of both the adolescent girl as well as her family.

Lifestyle modifications about diet, proper exercises etc are beneficial.

**Pharmacotherapy**: Treatment depends upon the pathophysiology and may be considered as follows:
• **For PCOS**: Lifestyle modification (BMI in the normal range), ovulation induction by Clomiphene citrate, HMG/HCG will bring regularity in menses and fertility; Metformin useful in girls showing signs of hyperandrogenism (improves menstrual cycle by its effect on insulin resistance reducing androgen levels).

**DYSFUNCTIONAL UTERINE BLEEDING AND PUBERTY MENORRAGIA**

Dysfunctional uterine bleeding is usually associated with anovulatory cycles. Bleeding is painless and often irregular (in the amount of bleeding, duration of period or in the interval between two periods). The causes are as follows:

- **Anovulation**: The anovulation is either due to inappropriate maturation of hypothalamus or persistent anovulation with high LH due to ovarian immaturity. Other causes may be PCOS, drugs, stress, excessive exercise etc.
- **Blood dyscrasias**: Idiopathic thrombocytopenia (ITP) is the most common cause. Thalassemia and Sickle cell anaemia may also be the causes of menorrhagia.
- **Anatomic lesions**: Trauma, foreign bodies (use of retained tampon), sexual abuse, cervical/endometrial polyp, leiomyoma, vaginal adenosis, rarely malignancies like endodermal sinus tumour, adenocarcinoma and rhabdomyosarcoma.
- **Hypothalamic factors**: Stress, eating disorders, excessive exercise, low body fat, psychosocial problems etc.
- **Immunology**: Ovarian antibodies and FSH/LH levels, antibodies against zona pellucida, ooplasm, theca cells, granulose cell etc.
- **Pregnancy complications**: Abortion, ectopic pregnancy, hydatidiform mole, retained products of conception etc.
- **Infection**: Cervicitis/vaginitis, PID
- **Systemic diseases**: Thyroid dysfunction showing signs of hyperandrogenism improves adrenal disorders, diabetes mellitus, hepatic dysfunction, renal dysfunction etc.
- **Latrogenic medications**: Tranquillisers, OCPs, anticoagulants, aspirin/NSAIDs, anti-neoplastic drugs, anti-seizure medications etc.

**Clinical Features of DUB**

- **History**: The age of menarche and a detailed menstrual calendar should be evaluated. A detailed history including the colour and quality of bleeding, pelvic pain, diet, any weight loss, medical history of chronic diseases, medications, family history of bleeding disorder or endocrine disorder should be taken.

With increasing trend to earlier sexual activity, one may need to enquire into contraceptive and sexual history, post coital bleeding, vaginal discharge etc. Pregnancy related causes must be ruled out. Use of hormones, such as OCPs or progesterone and use of other medications should also be enquired into.

Symptoms of anaemia, as well as indicators of coagulation disorders (bruising, epistaxis or gum bleeding) should be evaluated. Recent social stressful events, weight changes and a family history of menstrual disorders should be taken into account. All the pubertal milestones (thelarche, pubarche, adrenarche, menarche and overall body growth) should be evaluated to assess the maturational state of Hypothalamic-Pituitary-davian (HPO) axis. Presence of chronic illnesses, especially Tuberculosis must be enquired.

- **Examination**: Very young girl should be examined in presence of her mother or close relative.
- **General examination**: It includes the estima-
tion of body habitus, stage of secondary sexual characters and bleeding disorders. Evidence of acne and/or hirsutism would alert to the diagnosis of PCOS or adrenal problems. General assessment for endocrine diseases, vital signs for severe anaemia, tanner staging, thyroid palpation, assessment of vulva, hymen and pelvic organs are all checked for DUB assessment.

- **Abdominal examination**: It should be performed to rule out pregnancy or neoplastic diseases. At times, a pelvic examination needs to be performed (gently with one finger) to palpate the cervix and fornices. A per vaginal examination can also be quite useful.

**Investigations**

- **Pelvic ultrasonography**: It is helpful in the diagnosis of PCOs, uterine fibroid, ovarian cyst etc.
- **Laparoscopy/hysteroscopy/vaginoscopy**: These may be required in some girls to confirm the diagnosis.
- **Blood**: CBC, thyroid profile, serum LH/FSH, Androstenedione, pregnancy test, bleeding test, clothing time, prothrombin time; Pap smear and vaginal culture is performed in sexually active girls.

**Management of DUB**

The objective of treatment is to halt bleeding and prevent recurrences.

- **General**: If anaemia is present, proper treatment should be started. Proper healthy diet including whole grains, fresh fruits and avoiding saturated fats and commercial junk foods are advised. Supplementation with vitamin A, E, C and flavonoids (protect capillaries from damage) are helpful.
- **Mild cases**: These cases need supportive treatment. A confident reassurance and explanation of physiology will alleviate the anxiety of both the girl as well as her mother to a great degree. She should be educated about proper diet, exercise and stress management.

**Severe cases**: In severe cases and cases associated with anaemia, a hormone therapy is indicated. For quick arrest of heavy bleeding, the following need to be considered:

- A bolus dose of IV oestrogen (Progynon depot or Premarin 25 mg) is very effective or
- OCP (containing 0.05 mg: oestrogen) 1 pill every 6 hours, till bleeding stops and then gradually tapered to 1 pill every day. If bleeding is not stopped within 48 hours, one must look for causes other than anovulation. Oestrogens stop bleeding by enhancing platelet aggregation, increasing fibrinogen levels, increasing factor V as well as IX and decreasing effectiveness of bradykinin. Once bleeding is arrested, the patient should be prescribed cyclical OCPs or cyclic Progestins. The OCPs may be started at 1 tablet thrice a day for 4 days and then gradually tapered to 1 every day given cyclically for additional 2 months. In the event of non-response to hormonal therapy, one needs to reevaluate the case for presence of a coagulopathy or an anatomic disorder.
- Sometimes for arrest of acute bleeding, use of 2 testosterone injections 12 hours apart may be useful, once the bleeding stops or significantly reduces in quantity, oestrogen, progesterone or a combination is started. 

Hospitalisation is necessary in situations of acute or heavy bleeding with altered vital signs. Blood transfusion may be required, when haemoglobin levels are below 7 gm/dl.

To prevent heavy bleeding in a crisis situation, especially in presence of blood dyscrasias, Desmopressin nasal spray (dose 1.5 mg/ml) or 0.3 mg/kg
diluted in 50 ml of normal saline (administered over 15–30 minutes) may be life saving. It is a synthetic analogue of neurohypothalamic non-peptide arginine vasopressin. This results into a rapid rise of coagulation factor VIII with peak levels at 90 to 120 minutes and lasts for approximately 6 hours.

Prostaglandin synthetase inhibitors along with cyclical hormone therapy may be given with the start of menses. Mefenamic acid 500 mg or Tranexamic acid 1.5 mg may be given. In prolonged uncontrolled bleeding not responding to hormone therapy or when it is contraindicated, GnRH analogues can be given. These suppress gonadotropin secretion and subsequent oestradiol secretion, which stops menstruation completely and produces a state of amenorrhoea. Curettage is generally a last resort option to control bleeding. Balloon hemostasis may be required in some cases. Laparoscopic surgery may be required, if fibroids, ovarian cysts or endometriosis is present.

**CLINICAL APPROACH**

- More than two third of adolescent problems are related to menstruation.
- Dysmenorrhoea in adolescents is usually primary in nature.
- Counselling for lifestyle modifications, especially for exercise and diet are recommended. Healthy diet includes plenty of whole grains, fresh fruits and vegetables.
- Sympathy and politeness are very essential to ease the extreme anxiety of both the girl as well as her parents during evaluation.
- In a virgin girl with dysmenorrhoea, pelvic examination is not recommended and first line therapy with NSAIDs can be started.
- The most common presentation of abnormal uterine bleeding in adolescence is puberty menorrhagia, and anovulation is responsible for 80% of cases.
- Sometimes to control acute heavy bleeding, IV Oestrogen may be required.
- Reassurance, diet, exercise, stress management, healthy lifestyle play an important role.

**CONCLUSION**

In adolescent age group, menstrual problems are quite common. Dysmenorrhoea is one of the most frequently encountered gynaecological complaints in young women.

Puberty menorrhagia is the commonest presentation of abnormal uterine bleeding in adolescents. Anovulation is responsible in 80% of these cases. Careful management of each menstrual problem is essential. Good nutrition and healthy lifestyle play an important role in the adolescent girls. Diet supplemented with iron decreases excess menstrual blood loss in iron deficient girls, who have no other underlying cause/causes for their condition. Long term monitoring may be required in some girls with abnormal uterine bleeding. Usually a surgical option is not accepted easily by the young girl or her parents. Apart from the anxious parents we also need to keep in mind the long-term sequelae of therapy and the effects on reproductive carrier of the girl.

**About the Authors**

Dr Neeta Trohan and Dr Monika Sharma are Senior Demonstrator, Dr Anusuya Gehlot is a Professor, Dr Kamal Khichi is a Assistant Professor and Dr Poonam Jakhar and Dr Sahdev Choudhary are Resident, Department of Pharmacology, Dr SN Medical College, Jodhpur, Rajasthan.
INTRODUCTION

The term leucorrhoea or “vaginal whites” is applied to cases of abnormal vaginal discharge, non-haemorrhagic in nature, which is not caused by neoplasm or other serious organic disease. Leucorrhoea is one of the three most common complaints in obstetric and medical practice the other two being pain and haemorrhage. Women suffering from leucorrhoea experience psychological disturbance and matrimonial disharmony.

It is difficult condition to treat satisfactorily because of its uncertain aetiology. The treatment of leucorrhoea is both by oral and vaginal routes. However drawback associated with vaginal route includes:

- Administration requires privacy and professional supervision.
- Medicines do not spread evenly over the vaginal crevices and surfaces thus leaving some hidden infection which results in recurrence after a variable period of time.1–4

Incidence of Leucorrhoea in Indian Population

Desai et al and Agrawal et al reported leucorrhoea in 31% and 70% female population respectively.5,6 A community based study by Kulkarni et al, results suggest that presence of leucorrhoea is strongly associated with socio-economic and marital status, pregnancy
and parity of women. The incidence of leucorrhoea is more frequent in married female compared to unmarried, pregnant women compared to non-pregnant, women with high parity and women of lower socio-economic status (Figure 1). Married female are more prone to abnormal vaginal discharge due to sexual activity and frequent child bearing which leads to vaginal or sexually transmitted infections that in turn could lead to leucorrhoea.7

AETIOPATHOGENESIS OF LEUCORRHOEA

Various frequently encountered causes of a vaginal discharge are enlisted in Table 1. Vulvovaginitis (bacterial vaginosis, candida vulvovaginitis and trichomoniasis) is one of the most common cause leucorrhoea which shall be discussed in detail.8

The vulva, the external genitalia of the female, includes the labia majora and minora, the clitoris, and the vestibule of the vagina. During the reproductive years of a healthy woman’s life, the vagina maintains a moist environment that is in constant fluctuation. The secretion of an alkaline transudate from the vaginal epithelium and cervical glands maintains this moist environment with a pH ranging from 3.8–4.5. In addition, the vagina and its microflora form a unique balanced environment that can change under pressure from external stimuli but returns to normal with removal of the stimuli. It can vary in degree during the menstrual cycle, pregnancy, and sexual activity.

The vaginal epithelium consists of 3 cell layers: superficial, intermediate, and basal. These cells are capable of storing glycogen under the influence of oestrogen. Glycogen is available in the fully mature cells in the superficial layer of the epithelium. With elevated levels of either exogenous or endogenous oestrogen, all levels of the epithelium thicken as a result of glycogen storage. With diminishing levels of oestrogen, the layers become thin and atrophic.

In an adult woman’s reproductive years, the bacterial flora of the healthy vagina contains numerous microorganisms, including aerobic and anaerobic gram-positive and gram-negative bacteria (Figure 2). Lactobacillus and Corynebacterium predominate over other bacteria such as

Table 1. Causes of vaginal discharge8

<table>
<thead>
<tr>
<th>Category</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physiological</td>
<td>Pregnancy, Atrophic vaginitis</td>
</tr>
<tr>
<td>Sexually transmitted infections</td>
<td>Trichomonas vaginalis, Chlamydia trachomatis, Neisseria gonorrhoeae, Herpes simplex infection, Human papilloma virus, Human immunodeficiency virus (HIV)</td>
</tr>
<tr>
<td>Other infections</td>
<td>Vulvovaginitis (Candida species), Bacterial vaginosis, Yeast infections, Pelvic inflammatory disease</td>
</tr>
<tr>
<td>Neoplasm</td>
<td>Vaginal tumours, Cervical cancer, Endometrial tumours</td>
</tr>
<tr>
<td>Other</td>
<td>Drug induced (contraception pills, antibiotics, steroids), Foreign bodies or irritable (douches, scented soaps or lotions, bubble bath), Fistula, Dermatological conditions</td>
</tr>
</tbody>
</table>
Streptococcus, Bacteroides, Staphylococcus, and Peptostreptococcus. Both Lactobacillus and Corynebacterium produce lactic and acetic acid from glycogen, thus maintaining the low vaginal pH. Additional bacteria are kept in check by the acid-producing bacteria and are rarely pathogenic, but they may become pathogenic if the environmental balance is affected.

The skin of the vulva is sensitive to the vaginal environment and hormonal, metabolic, and allergic influences. It is composed of stratified squamous epithelium that contains hair follicles, sebaceous sweat glands, and apocrine glands.9,10

Pregnancy
In pregnancy increase numbers of glycogen-containing cells are discarded into the vagina due to hypertrophy of the vaginal epithelium. Women therefore notice an increase in vaginal discharge. Pregnant women are also predisposed to vaginal infections such as candida vulvovaginitis.8

Atrophic Vaginitis
Extremely low oestrogen production, as found after menopause or bilateral oophorectomy, can lead to atrophy of the vaginal and vulvar epithelium. Vulvovaginal atrophy is considered a natural process after oestrogen withdrawal; atrophic vaginitis, however, is not.

During the perimenopausal period, oestrogen secretion, primarily oestradiol, remains at approximately 120 ng/L. After menopause, it decreases to approximately 18 ng/L. The reduction of endogenous oestrogen causes thinning of the epithelium and a diminished glycogen content. Glycogen is necessary for rapid multiplication and maintenance of lactobacilli. The lack of glycogen contributes to a reduction in lactic acid production and an increase in vaginal pH, thus leading to the overgrowth of nonacidophilic species and the disappearance of Lactobacillus. In some patients, this new flora may include the introduction of bacteria that can incite a superficial infection in denuded regions and alter vaginal secretions.10

Vulvovaginal candidiasis
Vulvovaginal candidiasis is an acute, chronic, recurrent, or persistent condition that can involve the vulva, vagina, and adjacent areas. The specific causative agent belongs to the genus Candida. Candida is the most common causative agent for leukorrhea, affecting the women of all age group. Most of the non-albicans species of Candida are resistant to commonly used antifungal agent (azole). As per Aring et al candida infection results leukorrhea in 19% of the women with age of 21–30 years. Incidence of candidiasis was higher in pregnant (22.5%) compared to non-pregnant (16.6%).

Predisposing agents
Any host factor that affects the vaginal environment or vaginal secretions can play a role in the initiation of candida vulvovaginitis. Pregnancy is one of the most common predisposing factors.

- Women using high-dose oestrogens in oral contraceptives found an increase in vaginal colonization by Candida. The mechanism is believed to be similar to that found in pregnancy.
- Disorders associated with an altered immune response, such as acquired immunodeficiency syndrome (AIDS) and diabetes mellitus, also predispose to candida vulvovaginitis.
- Antimicrobials are thought to predispose a patient to Candida by reducing the number of protective resident vaginal bacteria. The most common offenders are broad-spectrum agents such as tetracycline, cephalosporins, and ampicillin like agents.

Clinical features
In acute vulvovaginal candidiasis, vulvar pruritus and burning are the main symptoms. Patients commonly complain of both symptoms after intercourse or upon urination. Physical findings include erythema and oedema of the vestibule and labia majora and minora. A thick, white, curd like vaginal discharge is usually present.

Clinical Features
Clinical symptoms include vaginal soreness, postcoital burning, dyspareunia, burning leucorrhoea, and occasional spotting. The most common symp-
tom is vaginal spotting, which usually results from a break in the thin vaginal mucosa. A serosanguinous discharge may be present, with a pH of 5–7. A wet mount often shows white blood cells and a paucity of Lactobacillus.\textsuperscript{10}

**Neoplasms**

A constant abnormal vaginal discharge always raises the suspicion of genital tract malignancy especially in the case of older women. The importance of a pelvic examination and regular cytological smears need to be explained to women.\textsuperscript{8}

**Drug Induced Leucorrhoea**

Drugs like oral contraceptive or drugs given through vaginal routes (vaginal creams and lubricants, douches, suppositories) may cause an allergic and inflammatory response in the vagina, or alter the hormonal environment. These drug are directly associated with an increased vaginal discharge. Chemical desquamation and secondary infection can also be caused by a variety of preparations.\textsuperscript{8}

**PHARMACOLOGICAL OPTIONS FOR MANAGEMENT**

Management of leucorrhoea can be tedious general practitioner and for the gynaecologist. The correct approach is to treat of underlying causes. How it will be treated will depend on what’s causing the problem. For example, if yeast is causative agent for leucorrhoea it is usually treated with antifungal medications inserted into the vagina in cream or gel form. Bacterial vaginosis induced leucorrhoea is treated with antibiotic pills or creams (Table 2).\textsuperscript{11}

Trichomoniasis is usually treated with the drug metronidazole or tinidazole. For atrophic vaginitis treatment includes topical vaginal oestrogen for 1–2 weeks. However, disadvantages include compliance issues due to the application process itself and its messiness. Hormone replacement therapy is not the only option for postmenopausal women.\textsuperscript{10}

**Herbal Therapy**

Physician or gynaecologist may consider nonpharmacological therapies, such as herbal treatments for management of leucorrhoea which has practically no side-effects. Herbal treatments are widely prescribed to women. A survey by the North American Menopause Society indicated that up to 10% of women use herbal therapies for menopausal symptoms and other gynaecological complaints.\textsuperscript{10}

Herbs are generally a harmless way to combat bacterial and fungal infection and to tone body system. As with any therapy, patient should consult health care provider before starting herbal treatment. Herbs can be used in different formulations like as in dried extracts (capsules, powders, teas), or tinctures (alcohol extracts). The following herbs may be useful for short-term treatment of leucorrhoea.\textsuperscript{12}

- **Glycyrrhiza glabra**: It has oestrogenic properties, smooth muscle depressant, anti-microbial, spasmolytic, antioxidant, anti-inflammatory.
- **Tribulus terrestris**: Different parts of *T. terrestris* have gram negative and gram positive antimicrobial activity. It is used as urinary anti-infective in Ayurvedic medicine and has antimicrobial activity.

**Table 2. Suggested treatment options for treatment vulvovaginal candidiasis**

<table>
<thead>
<tr>
<th>Treatment Options</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nystatin</strong>: Vaginal tablets 100,000 U qd for 14 d; ointment (100,000 U/g) bid for 14 d for vulvitis</td>
<td></td>
</tr>
<tr>
<td><strong>Miconazole</strong>: 2% vaginal cream qd for 7–10 d; 100-mg suppositories qd for 7 d; 200 mg suppositories qd for 3 d; 1200-mg vaginal suppository as a single dose; 2% cutaneous cream bid for 14 d</td>
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<tr>
<td><strong>Clotrimazole</strong>: 1% vaginal cream qd for 7–14 d; 100-mg vaginal tablet qd for 7 d; 500 mg suppository as a single dose</td>
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<tr>
<td><strong>Butoconazole</strong>: 2% vaginal cream qd for 3 d</td>
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<tr>
<td><strong>Terconazole</strong>: 0.4% vaginal cream qd for 7 d; 0.8% vaginal cream qd for 3 d; 80 mg suppository qd for 3 d</td>
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<tr>
<td><strong>Ketoconazole</strong>: 200–400 mg qd PO for 5 d</td>
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<tr>
<td><strong>Fluconazole</strong>: 150 mg tablet as a single dose</td>
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</table>
Antimicrobial and antifungal action against *S. aureus*, *B. subtilis*, *B. cereus*, *C. diphtheriae*, *E. coli*, *P. vulgaris*, *S. marcescens*, *S. typhimurium* and *C. albicans*.13

- **Asparagus racemosus**: (Antibacterial agent) - According to a study published in the African Journal of Traditional, Complementary and Alternative Medicine, the ethanol extract of dry powdered roots of asparagus was found to inhibit 18 strains of bacteria.14

- **Tinospora cordifolia**: It has a role in gynecological disorders and possesses anti-inflammatory properties.15

- **Withania somnifera**: Roots and leaves of *Withania somnifera* have antibiotic activity. It inhibits the growth of various Gram-positive bacteria, acid-fast and aerobic bacilli, and pathogenic fungi. It was active against *Micrococcus pyogenes var aureus* and partially inhibited the activity of *Bacillus subtilis* glucose-6-phosphat-edehydrogenase.16

A clinical trial on multi-herbal preparation containing *Valeriana wallichii*, *Glycyrrhiza* (Mulethi), *Mesua ferrea* (Nagkesar), *Areca catechu* (Supari), *Symlocos racemosa* (Lodh), *Tribulus terrestris* (Gokhru), *Phyllanthus emblica* (Amla), *Asparagus racemosus* (Shatavari), *Caesalpinia sappan* (Patang), *Tinospora cordifolia* (Giloe), *Withania somnifera* (Aswagandha), *Rauwolfia serpentina* was carried out by Gupta et al. As per this clinical trial, herbal preparation has demonstrated good clinical efficacy and safety profile in patients suffering from leucorrhoea and various other gynecological complications (Figure 3).2

Following observations were noted:

- The cases who had undergone D & C operation prior to the symptoms of leucorrhoea were treated with herbal drugs combination, and they got 100% cure. A feeling of well-being and restoration was observed in pregnant cases, when they were relieved of the symptoms of leucorrhoea.

- Similar results were also demonstrated by cases of vaginal hysterectomy and menorrhagia. In the latter group, the blood loss was less and duration also shortened.

- Tubal sterilisation cases also responded well after a single course of treatment; in 7 out of 9, complete cure was observed and two responded to a second course.

- Patients with specific lesions of erosion cervix and cervicitis responded well to herbal treatment.

- Chronic salpingitis leading to pelvic congestion and formation of cystic ovaries were probably responsible for backache which was relieved after 2 courses of herbal drugs combination at intervals of a fortnight.

- All the patients with complaints of weakness associated with leucorrhoea were cured after only one course for 3 weeks.

Figure 3. Multidisciplinary approach of herbal preparation in management of leucorrhoea and multiple complications
Out of 35 cases suffering from anaemia when the haemoglobin % was below 70%, the treatment was supplemented with oral antianaemic drugs. Unlike synthetic drugs where one specific molecule is utilised, in herbal remedies usually multiple molecules with vivid therapeutic effect are present.

Herbal remedies has practically no side-effects, even when used for a longer period of time, is easily available and easily acceptable.

CONCLUSION

Leucorrhoea or “Vaginal Whites” is applied to cases of abnormal vaginal discharge, non-haemorrhagic in nature, which is not caused by neoplasm or other serious organic disease.

Women suffering from leucorrhoea experience psychological disturbance and matrimonial disharmony.

Various frequently encountered causes of a vaginal discharge are pregnancy vulvovaginitis (bacterial vaginosis, candida vulvovaginitis and trichomoniasis), atrophic vaginitis, sexually transmitted infections, vaginal tumours and certain medications.

It is also difficult condition to treat satisfactorily in view of its uncertain aetiology. However treatment of leucorrhoea includes both pharmacological and non-pharmacological modalities.

Unlike synthetic drugs where one specific molecule is utilised, in herbal remedies usually multiple molecules with vivid therapeutic effect are present.

Herbal preparations are an inexpensive, effective and easily assessable treatment option is needed. The naturally occurring drugs are likely to fulfill all of these needs with better safety and tolerability profile compared to its synthetic counter parts.

About the Authors

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REFERENCES

Introduction
Rare obstetric entity diagnosis and management may pose some problems specially in low resource setting. Incidence of rudimentary horn pregnancy in bicornuate uterus is 1:76000 to 1:150000.1 It is usually seen in non-communicating horn of bicornuate uterus and hence rupture of pregnant horn with life threatening bleeding is possible. This is a case report of bicornuate uterus with non-communicating rudimentary horn pregnancy presenting initially as intrauterine foetal demise and later as failure of induction.

Management
Patient was posted for emergency laparotomy, after confirmation of Rudimentary horn pregnancy by MRI. Patient and her relatives were counselled about the same.

Laparotomy was performed under spinal anaesthesia. Findings at surgery were as follows: gravid enlarged pregnant rudimentary horn (non-communicating) right side. The horn was connected to right wall of left horn uterus (nonpregnant) with fibrous band just above the cervix (Figure 1). Left sided uterus had normal tube, ovary and cervix (Figure 2). Right sided gravid horn had normal tube and ovary. No evidence of rupture or haemoperitoneum seen. A macerated still birth weighing 850 gm male foetus was extracted from the horn. The rudimentary horn and ipsilateral tube was removed. The right ovary was conserved. Both the kidneys were palpated and found to be normal.

Abdominal closed in layers. Patient received two pints of whole blood post operatively. Her post operative recovery was normal. Stitches were removed on seventh post operative day. Histopathology report was suggestive of enlarged uterus with chorionic villi. No evidence of placenta percreta.

Discussion
Pregnancy in non-communicating horn of bicornuate uterus results through transperitoneal migration of sperm or fertilised ovum.2 The usual outcome of rudimentary horn pregnancy is rupture in second trimester in 90% of cases with foetal demise.3

Figure 1. Rudimentary horn with fibrous band just above cervix

Figure 2. Normal gravid horn with normal tube and ovary

RUDIMENTARY HORN PREGNANCY

Case of the Month
Woman at 24 Weeks of Gestational Age with Abdominal Pain and Loss of Foetal Movement
Varsha Desmukh, VY Kalyankar, Kanan Yelikar, PS Deshmukh, SM Rijhwani
In the present case, clinical features were suggestive of intrauterine foetal demise. Probably the diagnosis was initially missed on ultrasound due to poor index of suspicion. Two failed attempts of induction of labour made suspicion of extrauterine pregnancy which was confirmed by MRI.

The attachment of rudimentary horn with uterus varies from fibromuscular band to an extensive fusion between two horns where there is no external separation between them. The presence of fibromuscular band in this case made removal of gravid horn both easy and with minimal blood loss.

When rudimentary horn pregnancy is small and facilities exist it may be possible to resect it laparoscopically. Others have described the administration of methotrexate for termination of an early pregnancy in rudimentary horn followed by elective laparoscopic resection. Rudimentary horn pregnancy can be further complicated by placenta percreta due to poorly developed musculature, scant decidualisation and small size of horn.

It is interesting in this case why did the patient not present with haematometra earlier in her perimenarchal age. It may be due to endometrium in rudimentary horn is infantile and sometimes refractory to hormonal stimulation.

**Conclusion**

Pregnancy in rudimentary horn carries grave risk to the mother. There is a need of high index suspicion and increased awareness for early detection before rupture occurs. Excision of rudimentary horn with ipsilateral salpingectomy is the recommended surgical treatment and provides the best prognosis.

**References**


**About the Authors**

Dr Varsha Desmukh and Dr VY Kalyankar are Associate Professor, Dr Kanan Yelikar is Professor and Head of Department and Dr PS Deshmukh, Dr SM Rijhwani are Resident, Department Obstetrics and Gynaecology, Government Medical College, Aurangabad.
Prenatal Diagnosis in Conjoint Twins

Manu Goyal, Neeta Singh, Jai Bhagwan Sharma, Sunesh Kumar

INTRODUCTION

Multiple gestation complicates 1 in 80 pregnancies.1 After the establishment of assisted reproductive technology, the incidence of multiple gestation has increased a lot so as its associated complications. Conjoint twins is a rare entity and only few cases have been successful after the separation of two. It is very important to diagnose the anomaly antenatally by the ultrasonography (USG) and also to find the level of attachment in the twins and the vital organs shared between them.2 This will provide the information about the prognosis after surgery for the separation. If the vital organs are shared then the individual survival rate is very low and the couple should be offered termination after explaining the poor prognosis.

CASE SUMMARY

A 20 year old female G3P0+0+2+0 presented to gynaecology OPD with five months amenorrhoea and previous two miscarriages. It was her spontaneous conception. Her first trimester was uneventful and there was no USG done then. Patient brought a second trimester USG done at 20 weeks which showed conjoined twins attached ventrally at the level of thorax and upper abdomen (thoracopagus). There was single placenta, single umbilical artery in each twin and only one umbilical vein shared between twins. The hearts were separated only superiorly but were fused inferiorly and left and right ventricle shared between the twins. The anomaly would be incompatible to life, if twins were operated. The couple was explained poor prognosis and opted for termination of pregnancy. The patient was admitted in the labour room and tablet misoprostol 200 µg was instilled per vaginally twice at the interval of four hours. The patient aborted after 12 hours and placenta was also expelled. On examination of the abortus, there was conjoined thoracopagus, both females, weighed 464 grams with single placenta (Figure 1). The patient was discharged in stable condition on oral antibiotics. The autopsy was done on the fetus which confirmed the findings in antenatal USG. There was single ventricle of the heart and all other organs were normal.

DISCUSSION

Conjoined twins are identical twins who are joined together in utero. A rare phenomenon, occurrence range from 1 in 50,000 to 1 in 100,000 births, incidence being somewhat higher in South-east Asia and Africa.3 Approximately, half are stillborn and a small fraction of pairs are born alive with malformations incompatible to life.2 The overall survival rate for conjoined twins is approximately 25%. The condition is more frequently
found among females, ratio being 3:14. Conjoined twins are classified by the point at which their bodies are attached. The most common type is thoraco-omphalopagus (28%), followed by thoracopagus (18%) in which the twins are fused from upper thorax to lower belly and the heart is always involved in this.\(^5\) Surgery to separate the conjoined twins may range from simple to extremely complex, depending upon the point of attachment and the internal organs that are shared. Most cases of separation are risky and life-threatening.\(^5\) In many cases, surgery results in death of one or both twins, particularly if they are joined at the head. People have found the quality of life to be higher in twins who remain conjoined than is commonly supposed. Mortality rates for conjoined twins who undergo separation surgery vary. There are 68% chances of survival in twins who are fused at the level of sacrum, whereas in cases of twins with conjoined hearts at ventricular level, there are no known survivors. In the present case, twins were fused at the level of ventricles (pumping chamber), and the survival is very poor so the decision for termination of pregnancy was taken.

**CONCLUSION**

Pregnancy with twins should undergo detailed antenatal ultrasound examination in early weeks to know the type of twins and to diagnose conjoined twins, if there, so as to take the decision regarding continuation of pregnancy, since timely intervention prevents the complications and burden of carrying anomalous foetuses. Proper antenatal diagnosis and counselling of the couple is must for favourable outcome.

**About the Authors**

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**REFERENCES**

Developmental Language Disorder

Kate Nation, MA, DPhil

By the time most children go to school, the basic structural building blocks of language are well in place and they are able to use language to communicate appropriately with others in a variety of social settings. When one pauses for a moment to consider the complexities of language (Figure 1), it is truly remarkable that most children master it with such ease.

Some children, however, find language learning less straightforward. Concern over language development is one of the most common reasons for referral to health professionals during the preschool years, and language delay is associated with many developmental disorders such as autism and Down’s syndrome. In addition, there are some children who fail to acquire language normally, despite having normal intelligence and reaching other developmental milestones on time.

According to Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV), and International Classification of Diseases, 10th revision (ICD-10), criteria, the diagnosis of ‘developmental language disorder’ or ‘specific language impairment’ (SLI), previously known as developmental dysphasia, is applied when speech and language skills fall below non-verbal intelligence for no obvious reason; sensory impairment, gross neurological abnormality and pervasive developmental disorder, for example, are exclusionary criteria. SLI is a relatively
common developmental disorder, with an incidence estimated at between 3% and 10% of the population. Diagnosis usually involves a multidisciplinary assessment.\(^1\)

**BIOLOGICAL BASIS OF SLI**

**Genetic Factors**

There is clear evidence that SLI is a neurodevelopmental disorder that is transmitted genetically. It runs in families, and children are at greater risk of developing SLI if there is a family history of language impairment. Perhaps the strongest evidence for a genetic link comes from studies of twins: a number of studies have now demonstrated a much higher concordance for SLI between identical twins relative to that for non-identical twins. However, patterns of inheritance are complex.

Molecular studies have indicated potential regions of interest on chromosomes 16, 19, 13 and 3. Studies are consistent with the view that SLI is caused by multiple genes operating in a probabilistic manner, alongside multiple environmental risk factors.\(^1,2\) The pedigree of one family, the KE family, is consistent with a single dominant gene pattern of inheritance of speech and language impairment. Recent studies have located the affected gene (\textit{FOXP2}, a gene on the...
long arm of chromosome 7). It is important to note that this family is atypical. Nevertheless, the discovery of \textit{FOXP2} is an important milestone as it is the first gene to be identified that is implicated in speech and language disorder.4

There is clear evidence that SLI is a neurodevelopmental disorder that is transmitted genetically.

Brain Development
Although progress has been made at the genetic level, relatively little is known about the nature of brain development in SLI. Children with SLI make an interesting contrast to children who have acquired neurological damage. Most studies of young children with early focal damage find little evidence for subsequent language difficulties, even when the lesion involves substantial damage to the major areas implicated in language processing. Clearly, the plasticity seen in such children is not evident in children who go on to develop SLI.

The few imaging studies of SLI that have been conducted—alongside post-mortem studies of brain morphology—reveal remarkably few atypicalities in brain structure and organization. Moreover, some of the differences that have been reported (such as reduced leftward asymmetry of the planum temporale) are not specific to SLI, but have also been implicated in other disorders. A clear challenge for future research is to understand how genetic and environmental factors impinge on brain development in those with a neurodevelopmental disorder such as SLI.5

THE NATURE OF SLI

One of the major difficulties facing researchers and clinicians alike is that the behavioural manifestation of SLI varies enormously.

Speech and Language Difficulties
Some children with SLI have clear difficulties with speech and language. They may have unintelligible speech, or struggle to find the words they are looking for; many children with SLI make grammatical errors and fail to comprehend complex sentences. With respect to the language subsystems described in Figure 1, these children may have difficulty with phonology, grammar and semantics.
Difficulties with Language use

In contrast to these obvious speech and language impairments, some children have disproportionate difficulties with using language appropriately. Although their speech can be relatively well formed and intelligible, they have trouble participating in a conversation owing to problems with maintaining the thread of a topic or dealing with intended (as opposed to literal) meaning. Some (but not all) of these children may have mastered language form and structure, but are clearly struggling with those aspects of language involving pragmatics.

One approach to dealing with this heterogeneity has been to search for subtypes of SLI. (Table 1) Although this provides descriptive labels that may be useful clinically, the validity of proposing qualitatively distinct subtypes is far from clear. As SLI is a developmental disorder, its manifestations change over time, and it is not at all unusual to see children who would fit different subtypes at different points in time. Complicating factors include severity, the amount of intervention received, and other strengths and weaknesses an individual child may possess (in general cognitive ability, for example).

### Table 1. Varieties of developmental language development

<table>
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<tr>
<th>DSM-IV and ICD-10</th>
<th>Mixed expressive and receptive disorder</th>
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<td></td>
<td>Children have difficulty with both producing and comprehending language. Utterances tend to be short and error-prone (in terms of both phonology and grammar). Vocabulary is limited and understanding is poor, especially of complex sentences.</td>
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<tr>
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<th>Expressive language disorder</th>
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<td>Mutually exclusive from mixed disorder: language difficulties seem more restricted to language expression rather than language comprehension. However, most children with expressive difficulties are thought to have subtle problems with comprehension if tested using sufficiently sensitive tests.</td>
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<td>It is not clear whether these two diagnostic categories are qualitatively distinct rather than different points on a continuum of severity. There has been a move in the literature to describe a child's difficulty in terms of the domains of language (see Figure 1) they find most troublesome, rather than forcing a distinction to be made between receptive and expressive abilities. As discussed in the text, however, these are currently descriptive subtypes rather than valid diagnostic categories:</td>
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<td><strong>Grammatical SLI</strong></td>
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<td>Children who have disproportionate difficulties with grammar, especially with word order, tense and agreement marking, as well as with producing and comprehending complex sentences. Other aspects of language, although impaired, are relative strengths compared with grammatical abilities.</td>
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<td></td>
<td><strong>Word-finding difficulties</strong></td>
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<td>Production of speech sounds is relatively normal in terms of phonology and grammar, but the child has difficulty finding the appropriate word, and as a consequence, language production is impoverished and immature. Comprehension is usually impaired, but perhaps to a lesser degree.</td>
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<td></td>
<td><strong>Semantic pragmatic impairment (or pragmatic language impairment)</strong></td>
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<td>Although the child may produce complex, fluent and well-formed sentences, language is not really used for social communication. Utterances can be verbose or over-formal, and have a bizarre or odd quality, similar to the language of some children with autistic spectrum disorder. Vocabulary and grammar can be relatively strong, but comprehension of extended discourse is poor. Non-verbal communication weaknesses are also apparent (eg, lack of eye contact, poor turn-taking skills, unusual intonation).</td>
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<td><strong>Phonological disorder (DSM-IV) or specific articulation disorder (ICD-10)</strong></td>
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<td>Although the child’s use of speech sounds is below appropriate level, language skills are normal. The difficulties should be linguistic in nature and not due to structural impairment (eg, cleft palate) or motor difficulties (when a diagnosis of dysarthria or dyspraxia may be appropriate).</td>
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<tr>
<td></td>
<td><strong>Acquired aphasia with epilepsy (Landau–Kleffner syndrome)</strong></td>
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<td></td>
<td>Following normal progress in language development, language regresses, causing severe receptive and expressive impairments. Usually associated with atypical electrical activity in the temporal lobes.</td>
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It is generally agreed that SLI is a heterogeneous disorder, but there is as yet no objective rationale for defining subtypes, and in most studies, it is treated as a unitary disorder.
It is generally agreed that SLI is a heterogeneous disorder, but there is as yet no objective rationale for defining subtypes, and in most studies, it is treated as a unitary disorder.

**THE UNDERLYING NATURE OF SLI**

Partly in response to the desire to identify the heritable phenotype of the disorder, efforts have been made to specify the cognitive mechanisms underpinning SLI. A number of hypotheses have been proposed, all of which have received some support from experimental investigations, but, as yet, there is no conclusive evidence to suggest that any of these factors is the single underlying cause of SLI.

- One prominent view sees SLI as an impairment caused by a general limited temporal processing capacity. This deficit has a huge impact on speech and language development as the child will have difficulty dealing with speech sounds, which tend to be very rapid and short in duration.

- An alternative account proposes that children with SLI have a limited phonological short-term memory (the system responsible for maintaining active representations of speech sounds for short periods of time) and that this hampers language learning.

- A third account argues that SLI is a consequence of an underlying deficit in the system responsible for the representation of grammar.

There are the beginnings of a move away from the view that there is a single cause of SLI to one that assumes multiple risk and protective factors contribute to the manifestation of SLI. Behavioural genetic evidence suggests that poor phonological short-term memory and problems with grammar index separate genetic risks, additionally, individuals at genetic risk may go on to have a clinical language impairment only if other risk factors—whether environmental or genetic—are also present.

One consequence of studies addressing the search for the heritable phenotype is that efforts are being made to evaluate the validity of diagnostic tests in terms of sensitivity and specificity. Given increasing dissatisfaction with current clinical diagnostic categories, research of this nature will help us to understand the complex aetiology of SLI more fully and should help to specify better methods of assessment and intervention.

**PROGNOSIS**

Many children who present with poor language in the preschool years are best described as late developers who, after a slow start, make good progress and soon ‘catch up’ with their peers. This observation presents a number of ethical and practical challenges to the clinician.

- Should all preschoolers with language delay receive therapy?
- If not, how do we decide who should receive treatment and who should not?
- When does a ‘normal’ late developer become a child with a clinical language impairment?

A number of longitudinal studies have attempted to distinguish transient from persistent impairment. For example, Bishop and Edmundson found that, of a clinical sample of 4-year-olds with normal non-verbal ability but poor language (most of whom were receiving some speech therapy), 44% had resolved by the time they were 5.6 years old. Although these findings are encouraging, suggesting that many problems appear to resolve in time and with early intervention, there is a need for caution. When the sample was later recruited at age 15 years, the children whose language skills had resolved by 5.6 years, nevertheless, had poorer literacy skills than controls, did less well in formal examinations and had subtle weaknesses on some language measures.

For children whose speech and language impairments do not resolve by mid-childhood, continuing and persistent language difficulties seem to be the norm.
generally, children with SLI achieve low levels of educational success. In addition to academic failure, children with speech and language difficulties are at risk of the following:

- Behavioural problems, such as poor attention and conduct disorder
- Psychosocial problems, including depression and anxiety
- Poor self-concept
- Rejection by peers

**SLI and Other Problems**

Common co-morbidities include reading disorder and motor disorder. Around 50% of children with language impairment have some degree of emotional, behavioural or psychiatric difficulty. Turning this finding around, Cohen\(^3\) assessed the language skills of children presenting with primary psychiatric symptoms. After excluding children with known language impairment, sensory impairment or autism spectrum difficulties, 34% of the sample met the criteria for SLI. These children with unrecognized SLI tended to have relatively good expressive language abilities, so their adequate speech may have masked their poor language comprehension.

An important cautionary finding from Cohen’s study is, therefore, that good speech should not be taken as an index of good language, and that children presenting with complex emotional, behavioural or psychiatric problems may have underlying language difficulties that have not been recognized. These children seem to be at particular risk of depression, and of developing aggressive behaviour.

Although there is a strong association between language difficulties and psychopathology, group data mask considerable individual variation, and the nature and origins of the complex and varied relationship continues to be debated. Co-morbidity is potentially a consequence of common neurodevelopmental immaturities, or one disorder could increase the risk of another, either concurrently or later on.

The importance of developmental change has been highlighted by a number of longitudinal studies documenting both the long-term prognosis of children with SLI and how the pattern of difficulties changes over time.\(^{14–16}\) These studies show that, by adulthood, those with a
history of SLI are at risk of experiencing substantial social problems, similar in nature to those seen in autism spectrum disorders, demonstrating very clearly the persistent and complex problems experienced by people with developmental language disorders. At a practical level, they highlight the need for greater help and support than is generally available.


About the Author
Professor Nation is Professor of Experimental Psychology at the University of Oxford and a Fellow of St John’s College, Oxford, UK. Her research interests include the development of language and literacy, both in normal and atypical development, and she has particular interest in children’s language comprehension difficulties.

Further Reading
4. Norbury CF, Tomblin JB, Bishop DVM, eds. Understanding developmental language disorders. Hove, UK: Psychology Press; 2008. (The two references above are collections of papers concerned with the key topics in understanding and treating developmental language impairments.)

What’s new
• Recent studies exploring the aetiology of developmental language disorder suggest that it is heterogeneous in nature and origin.
• Longitudinal studies have revealed complex and mixed outcomes in adolescence and adulthood.

REFERENCES

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