Associated Infections in Persistent Diarrhoea—Another Perspective

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Summary

Seventy-eight children diagnosed as cases of persistent diarrhoea (PD) from 1 month to 5 years of age (mean age 8.92 months) hospitalized during a 2-year study period were screened for the presence of non-gastrointestinal infections. Clinical screening suggested acute respiratory infection (ARI) in 30 per cent cases, urinary tract infection (UTI) in 19 per cent and acute suppurative otitis media (ASOM) in 10 per cent of cases. Investigations revealed pneumonia on chest X-ray (39 per cent), positive urine culture (32 per cent), leucocytosis (31 per cent) and positive blood culture (22 per cent). Seven cases (9 per cent) of pneumonia and 10 cases (13 per cent) diagnosed to have UTI were not identified on clinical screening and could be detected only after investigations. E. coli was the commonest organism isolated from urine culture (23 per cent) and blood culture (14 per cent); 54 per cent of cases had one or the other associated infection and 28 per cent were suffering from more than one infection. Bacterial pathogens were more frequently isolated from blood in children <6 months (P<0.01), with vomiting (P<0.001), and severe malnutrition (P<0.05); from urine in association with fever (P<0.001), duration of diarrhoea > 4 weeks (P<0.05), and vomiting (P<0.001). Pneumonia was detected on chest radiograph more frequently in children with severe malnutrition (P<0.001). Sixty eight per cent of cases were successfully treated with dietary management and appropriate treatment of associated infections and 18 per cent of cases died. Mortality was highest in association with severe oral thrush, severe malnutrition, septicaemia, and ARI.

Our results suggest that majority of cases of PD are associated with one or the other non-gastrointestinal infections particularly UTI and ARI which may be missed on clinical examination unless efforts are made to investigate these children. Early detection and appropriate management of these infections can considerably modify hospital course and outcome.

Persistent diarrhoea (PD) is a common problem in the developing world since 3-20 per cent of acute diarrhoeal episodes in children less than 5 years become persistent. Nutritional rehabilitation has remained the mainstay of management of PD. During the last decade much work has been done to identify and treat persistent gut infection and attempts have been made to evaluate various diets during PD for nutritional rehabilitation. Lately, increasing evidence of associated non-gastrointestinal infections has been reported. A thorough clinical screening for such infections and their appropriate treatment has been observed to greatly influence the course and prognosis of PD. This study has been undertaken to estimate the magnitude, the clinical spectrum and management of associated infections in hospitalized cases of PD.

Materials and Methods

Children of either sex below the age of 5 years admitted to the Diarrhoea Training and Treatment Unit (DTU) of Kalawati Saran Children's Hospital, New Delhi from January 1992 to December 1993 were studied. On admission a detailed history was taken including identification of risk factors for PD. Besides screening for vitamin deficiency, a thorough search was made for detection of non-gastrointestinal infections. All admitted cases were subjected to complete blood count and culture, routine urine examination and culture, mantioux test, chest X-ray, stool for ova or cyst, fecal leucocytes, and red blood cells, and culture.

Dehydration was assessed and treated as per recommended guidelines. Children over 4 months of age were initially given lactose reduced diet (milk + cereal/yoghurt). If there was no improvement in frequency and volume of stool after 72 hours, a lactose-free diet (lentil + cereal) was introduced. If there was no improvement after 72 hours comminuted chicken feeds were started. Breast-fed children continued to be breast-fed along with one of these diets. In infants less than 4 months of age yoghurt was used initially as lactose reduced diet. If there was no response then casein-based lactose-free feeds were given. If there was no improvement after 72 hours comminuted chicken feeds were started. Cases with bloody diarr-
Results

Seventy-eight children from 1 month to 5 years of age (mean age 8.92 months) with 44 infants (56 per cent) less than 6 months, 28 (36 per cent) between 7 and 24 months, and six children (8 per cent) more than 2 years of age were admitted in the DTU over a 2-year study period. Forty-five were males (58 per cent) and 33 females (42 per cent) with duration of diarrhoea ranging from 14–28 days (89 per cent), 29–60 days (6 per cent) to more than 60 days (5 per cent). Eighteen per cent of cases had history of recurrent episodes of acute diarrhoea and 21 per cent of cases had previous history of PD. Only eight out of 44 infants less than 6 months of age (18 per cent) were exclusively breastfed. On examination 26 cases (33 per cent) had normal nutritional status, 21 (27 per cent) mild PEM, 16 (21 per cent) moderate PEM, and 15 children (19 per cent) had severe malnutrition. Forty-three children (55 per cent) had no dehydration at the time of enrolment, 27 (35 per cent) had some dehydration and eight (10 per cent) had severe dehydration. Other associated clinical features included anaemia (51 per cent), fever (39 per cent), vomiting (22 per cent), dysentery (19 per cent), vitamin A deficiency (15 per cent), oral thrush (14 per cent), and pyoderma (8 per cent). Acute respiratory infection (ARI) was clinically diagnosed in 30 per cent of cases, but chest radiograph showed evidence of pneumonia in 39 per cent. Urinary tract infection (UTI) and acute suppurative otitis media (ASOM) were clinically suspected in 19 and 10 per cent of cases, respectively (Table 1). Stool microscopy revealed cysts/trophozoites of Giardia lamblia (15 per cent) and E. histolytica (9 per cent), polymorphonuclear leucocytes >5/hpf in 39 (50 per cent), and red blood cells in 20 children (26 per cent). Enteropathogens isolated from stool culture included E. coli (24), Shigella (10), Salmonella (6), Aeromonas (2) and Pleisomonas (2). Due to lack of facilities it was not possible to perform the serotyping of E. coli. Bacterial pathogens were isolated from urine culture in 25 children (32 per cent) and from blood culture in 17 cases (22 per cent). E. coli was the commonest organism isolated from blood and urine culture (Table 2). Most of our patients (54 per cent) had one or the other non-gastrointestinal infection. Twenty-two children (28 per cent) were suffering from more than one infection. Age <6 months, diarrhoeal duration >4 weeks and fever seemed to be more frequently associated with non-gastrointestinal infections (Table 3). With dietary management and appropriate treatment for associated infections 53/78 cases (68 per cent) improved in their clinical condition and diarrhoea was controlled within 3–10 days. 11 cases (14 per cent) continued to pass loose stools before leaving the hospital and 14 (18 per cent) expired. Mortality was highest in association with severe oral thrush (73 per cent) followed by severe malnutrition (67 per cent), septicaemia (65 per cent), pneumonia (40 per cent), stoll polymorphonuclear leucocytes >5/hpf (28 per cent), and with positive urine culture (24 per cent).

Discussion

Infection and PD are very closely related. Impaired immunological response due to IgA deficiency\(^{1,2,13}\) and impaired cell-mediated immunity\(^{3,13,14}\) has been incriminated as causative factors for prolongation of diarrhoeal episodes. Increased frequency of PD in association with Aids\(^{15}\) further supports this view. Baqui et al.\(^{16}\) have suggested that cell-mediated immune deficiency and malnutrition are independent risk factors for PD. Several studies have focused their observations on continuation of mucosal injury due to bacterial overgrowth\(^{17,18}\) and persistence of gastrointestinal infection particularly by some of the enteropathogens like entero-adherent aggregative E. coli\(^{2,3,19,20}\) and cryptosporidium.\(^{4,19}\) However, more recently, frequent association of PD has been noticed with UTI or ARI or both.\(^{6}\) Our results suggest that majority of our cases (54 per cent) were associated with one or the other non-gastrointestinal infections. The commonest infections were UTI, ARI, and ASOM. It was an interesting observation that 10 cases of UTI (13 per cent) and seven of pneumonia (9 per cent) were diagnosed only after investigations. These cases were missed on clinical screening and therefore highlight the

<table>
<thead>
<tr>
<th>Infections suspected/detected</th>
<th>No. of cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical screening</td>
<td></td>
<td></td>
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<tr>
<td>Acute respiratory infection</td>
<td>23</td>
<td>29.5</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>15</td>
<td>19.2</td>
</tr>
<tr>
<td>Oral thrush</td>
<td>11</td>
<td>14.1</td>
</tr>
<tr>
<td>Acute suppurative otitis media</td>
<td>9</td>
<td>10.2</td>
</tr>
<tr>
<td>Laboratory investigations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal chest radiograph</td>
<td>30</td>
<td>38.5</td>
</tr>
<tr>
<td>Positive urine culture</td>
<td>25</td>
<td>32.1</td>
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<tr>
<td>Leucocytosis</td>
<td>24</td>
<td>30.8</td>
</tr>
<tr>
<td>Positive blood culture</td>
<td>17</td>
<td>21.8</td>
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TABLE 2
Organisms isolated from blood/urine culture

<table>
<thead>
<tr>
<th>Organism</th>
<th>Blood culture No. of cases</th>
<th>Urine culture No. of cases</th>
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<tbody>
<tr>
<td></td>
<td>Percentage</td>
<td>Percentage</td>
</tr>
<tr>
<td>E. coli*</td>
<td>11</td>
<td>18</td>
</tr>
<tr>
<td>Klebsiella**</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Proteus</td>
<td>—</td>
<td>1</td>
</tr>
<tr>
<td>Salmonella</td>
<td>3</td>
<td>—</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>Staph. aureus</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>Citrobacter</td>
<td>—</td>
<td>1</td>
</tr>
<tr>
<td>Acinetobacter</td>
<td>—</td>
<td>1</td>
</tr>
</tbody>
</table>

*Isolated from blood as well as from urine in nine cases (12 per cent).
**Isolated from blood as well as from urine in one case (1 per cent).

TABLE 3
Correlation of clinical parameters with associated infections

<table>
<thead>
<tr>
<th>Clinical/laboratory parameters</th>
<th>Correlation with**</th>
<th>Sen.** (%)</th>
<th>Spe. (%)</th>
<th>+ PV (%)</th>
<th>— PV (%)</th>
<th>Odds ratios</th>
<th>$x^2$</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt;6 months</td>
<td>PCR</td>
<td>45.5</td>
<td>70.6</td>
<td>66.7</td>
<td>50.0</td>
<td>2.0</td>
<td>1.46</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>PUC</td>
<td>36.4</td>
<td>73.5</td>
<td>64.0</td>
<td>47.2</td>
<td>1.6</td>
<td>0.46</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>PBC</td>
<td>34.1</td>
<td>94.1</td>
<td>88.2</td>
<td>52.5</td>
<td>8.3</td>
<td>7.37</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Fever</td>
<td>PCR</td>
<td>53.3</td>
<td>70.8</td>
<td>53.3</td>
<td>70.8</td>
<td>2.8</td>
<td>3.59</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>PUC</td>
<td>56.7</td>
<td>83.3</td>
<td>68.0</td>
<td>75.5</td>
<td>4.7</td>
<td>11.78</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>PBC</td>
<td>30.0</td>
<td>83.3</td>
<td>52.9</td>
<td>65.6</td>
<td>2.1</td>
<td>1.22</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Duration of diarrhoea &gt;4 weeks</td>
<td>PCR</td>
<td>66.7</td>
<td>65.2</td>
<td>20.0</td>
<td>93.7</td>
<td>3.6</td>
<td>2.20</td>
<td>&gt;0.05</td>
</tr>
<tr>
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<td>PUC</td>
<td>66.7</td>
<td>72.5</td>
<td>24.0</td>
<td>94.3</td>
<td>5.3</td>
<td>3.94</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>PBC</td>
<td>33.3</td>
<td>79.7</td>
<td>17.6</td>
<td>90.2</td>
<td>2.0</td>
<td>0.21</td>
<td>&gt;0.05</td>
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<tr>
<td>Vomiting</td>
<td>PCR</td>
<td>47.1</td>
<td>81.3</td>
<td>26.7</td>
<td>81.3</td>
<td>1.6</td>
<td>0.29</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>PUC</td>
<td>82.4</td>
<td>82.0</td>
<td>56.0</td>
<td>94.3</td>
<td>21.2</td>
<td>21.67</td>
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<tr>
<td></td>
<td>PBC</td>
<td>58.8</td>
<td>88.5</td>
<td>58.8</td>
<td>88.5</td>
<td>11.0</td>
<td>14.81</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Severe malnutrition</td>
<td>PCR</td>
<td>86.7</td>
<td>73.1</td>
<td>43.3</td>
<td>95.8</td>
<td>17.6</td>
<td>15.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
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<td>PUC</td>
<td>53.3</td>
<td>73.1</td>
<td>32.0</td>
<td>86.8</td>
<td>3.1</td>
<td>2.74</td>
<td>&gt;0.05</td>
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<tr>
<td></td>
<td>PBC</td>
<td>46.7</td>
<td>84.1</td>
<td>58.8</td>
<td>86.9</td>
<td>4.6</td>
<td>5.05</td>
<td>&lt;0.05</td>
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<tr>
<td>Leucocytosis</td>
<td>PCR</td>
<td>45.8</td>
<td>64.8</td>
<td>36.7</td>
<td>72.9</td>
<td>1.55</td>
<td>0.40</td>
<td>&gt;0.05</td>
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<tr>
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<td>PUC</td>
<td>45.8</td>
<td>74.0</td>
<td>44.0</td>
<td>75.5</td>
<td>2.41</td>
<td>2.17</td>
<td>&gt;0.05</td>
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<tr>
<td></td>
<td>PBC</td>
<td>20.8</td>
<td>77.8</td>
<td>29.4</td>
<td>68.8</td>
<td>0.92</td>
<td>0.18</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

*PCR = Pneumonia in chest radiograph; PUC = positive urine culture; PBC = positive blood culture.
**Sen. = Sensitivity; Spe. = specificity; + PV = positive predictive value; — PV = negative predictive value.

need for careful screening of children with PD by all available means to rule out any associated sepsis elsewhere.

In 22 cases (28 per cent) more than one infection was associated. Most of these cases did not have a favourable outcome as 6/22 (27 per cent) did not improve and 12/22 cases (55 per cent) died. Mortality was highest in children with severe oral thrush, followed by severe malnutrition, septicaemia, multiple infection, and pneumonia. However, early diagnosis and prompt treatment of associated infection with appropriate antibiotics saved 82 per cent children and in 68 per cent of cases diarrhoea was controlled within a week of hospitalization.

Our results indicate that hospital stay and outcome of cases with PD is considerably modified by the presence of associated infections and that a thorough search for these infections and their prompt manage-
A. Sibal et al. ment are of paramount importance notwithstanding the dietary rehabilitation which remains the cornerstone of management of PD.

References