Isolation of \textit{campylobacter lari} from pediatric patients in King Khalid University Hospital

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\textbf{ABSTRACT}

Four cases from whom \textit{Campylobacter lari} were isolated from blood and/or stool specimens are reported. All the patients were aged less than 3 years, all presented with diarrhea, which was bloody in one case. None of the patients were immunocompromised. Isolation of \textit{C. lari} from the blood of such patients is not commonly encountered. The methods of isolation and identification of \textit{C. lari} are presented with a brief review of the literature.

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\textbf{Keywords:} \textit{C. lari}, gastroenteritis, bacteraemia, immunocompromised patients.

\textbf{S}kirrow and Benjamin were the first workers to report in 1980, the frequent isolation of \textit{Campylobacter laris} from wild seagulls of the genus \textit{larus} which has been renamed \textit{C. lari}. The organism was also isolated from other animals and man by the same authors although less frequently. Deoxyribonucleic acid (DNA) analysis studies showed that \textit{C. lari} belongs to the group of nalidixic acid resistant thermophilic \textit{campylobacter} species (NARTC). The first report of its potential pathogenicity for humans came in 1984 when Nachamkin et al. reported the first case of \textit{C. lari} bacteremia from an immuno-compromised patient. We report the isolation of \textit{C. lari} from the blood and/or stool of four immunocompetent children who presented with diarrhea. Isolation of \textit{C. lari} from blood of non-immunocompromised patients is not a common finding. \textit{C. lari} has been reported very rarely as a cause of diarrhea in humans. Medical literature on the epidemiological and pathogenesis of \textit{C. lari} in the Middle Eastern countries is lacking. To the best of our knowledge this is the first report on \textit{C. lari} from the Middle East in general and Saudi Arabia in particular.

\textbf{Case Reports}

\textbf{Case no. 1} A two day old baby girl presented at the Neonatal Intensive Care Unit (NICU) at King Khalid University Hospital with bloody diarrhea. She was born at full term to a 32-year old Bangladeshi lady. The birth weight was 3.320 kg. Pregnancy and delivery were uneventful. Physical examination was unremarkable. A full septic work-up was carried out on admission which included blood and stool cultures. Radiography revealed no abnormality. She was empirically started on ampicillin and gentamicin. Next day she was well and had no more bloody diarrhea. Seventy-two hours later she was discharged from the NICU. On day 7 the blood culture, collected on admission, was positive. Gram stain of the isolate showed a gram negative curved bacillus which was later identified as \textit{C. lari}. Stool culture revealed the same organism. Accordingly, the patient was readmitted to the ward and had a full septic work-up including repeat stool and blood cultures and was put on gentamicin therapy for 10 days. During this period she remained symptom-free. Her mother's stool and blood cultures were negative for \textit{C. lari}. Repeated stool and blood cultures were negative. The patient was discharged home in good health.

\textbf{Case no. 2} An 18-month old Saudi boy presented at the Pediatric Clinic at King Khalid University Hospital with recurrent episodes of diarrhea for 2 weeks. Details of patient's history were not relevant except for contacts with pet birds at home. Physical examination showed no abnormality and laboratory investigations were unremarkable. A stool specimen was positive for \textit{C. lari}. The blood culture was negative. No
treatment was given. The patient was followed up for 8 weeks and he was thriving well.

Case no. 3 An 11-month old Saudi girl presented at the Pediatric Emergency Clinic at King Khalid University Hospital with a history of watery diarrhea and poor feeding for two days. There was no fever and no other constitutional symptoms. She was fully vaccinated. Physical examination was unremarkable. Stool culture was positive for *C. lari*. Blood cultures were negative. No treatment was given. Follow-up of the patient for 4 weeks revealed no abnormality.

Case no. 4 A 2 1/2-year old Saudi girl presented at the Pediatric Clinic at King Khalid University Hospital with a history of watery diarrhea three to four times a day for two days. The diarrhea was associated with abdominal pain on passing stool. There was no blood or mucus in stool, no fever or other constitutional symptoms. Physical examination and laboratory investigations were unremarkable. Stool culture was positive for *C. lari* and blood cultures were negative. The patient was sent home on no treatment. Later on the patient was seen in the clinic and she was well.

**Microbiological investigations** Paired blood cultures, aerobic and anaerobic were performed on each patient in Bactec 9240, bottles (Becton Dickinson, Maryland, USA). They were subcultured when showing signs of growth (when indicated by the machine) on blood and chocolate agar and incubated at 37 °C. Stools were cultured on blood agar, a *campylobacter* Skirrow’s selective medium and other media for enteric pathogens. *Campylobacter* medium was incubated at 42 °C in a microaerophilic atmosphere using a gas pack jar. For identification, subculture was made on blood agar and incubated at 25 °C, 37 °C and at 42 °C in a microaerophilic atmosphere. The organisms were identified as *C. lari* by their ability to grow at 37 °C and 42 °C, failure to grow at 25 °C, characteristic colonial morphology, positive oxidase and catalase reactions, negative hippurate hydrolysis, H2S production and resistance to nalidixic acid and cephalothin. Antimicrobial susceptibility was performed using Stoke’s comparative disc diffusion technique. A known *campylobacter* species strain was used as a control. All the organisms were found to be sensitive to erythromycin, ampicillin, gentamicin and resistant to cefoxime, ceftriaxone, cefotaxime and tetracycline. Minimum inhibitory concentration (MIC) determination was also performed on the blood isolate from case No. 1 by E-test (AB Biodisk, Solona, Sweden) against erythromycin, gentamicin and ampicillin. The MIC was 0.190 µg/l, 0.023 µg/l and 0.50 µg/l respectively.

**Discussion** Members of the genus *Campylobacter* are well established etiologic agents of human diarrheal disease particularly *C. jejuni*, *C. coli* and *C. fetus*.[2,4-9] Several studies have been conducted in children and adults on *C. jejuni enteritis* in Saudi Arabia.[2,4-9] In recent years, many studies reported the association of *C. lari* with gastroenteritis and bacteremia.[2,4,10,12] This is the first report of infection due to *C. lari* from our institution and probably from Saudi Arabia and the Middle East. *C. lari* was most frequently isolated from feces of wild seagulls and occasionally from a variety of other birds, mammals and water.[1] The DNA hybridization studies showed *C. lari* to belong to the group of nalidixic acid resistant thermophilic *Campylobacter* species (NARTC).[2,3] Few studies have been conducted on the pathogenesis of *C. lari*.[10]

Previously reported cases of *C. lari* showed that *C. lari* was isolated either from blood in patients with bacteremia or from the stool in patients with gastroenteritis or both.[2,4,10-18] In one case *C. lari* was isolated from the appendix of a child with acute appendicitis.[13] Reported cases of *C. lari* included both adults and children (8 months - 70 years). Unlike our cases, some of these patients were immunocompromised, some had chronic diseases, while some were AIDS patients.[1,10,14,15] The tendency of *C. lari* to cause disease was found to be due to the production of both cytotoxic and cytopathic factors as determined by Johnson and Lior.[10] Cytotoxic factors were detected from all human isolates compared to only half from non-human isolates.[10] The same authors suggested other factors such as colonization ability, invasiveness and host resistance to be important in the pathogenesis of diseases due to *Campylobacter* species.

Most of the patients having *campylobacter* species bacteremia, previously reported, suffered from chronic underlying diseases.[2,3,11,14,15,19] On the contrary none of our four patients had any underlying medical problem. The source of infection in our cases was not clear, although a history of contact with a pet bird at home was given in one case. Other sources, for example, water supply or food could not be confirmed because none of their family members complained of diarrhea. Gentamicin was given to the patient with *C. lari* bacteremia, however, the other three patients with *C. lari* gastroenteritis were systemically well and therefore were not treated. They did not have symptoms on further follow-up. Therefore, our results showed that *C. lari* bacteremia patients can be treated with gentamicin. As *C. lari* gastroenteritis is self-limiting, treatment is not recommended. However, if the patient is systemically ill, erythromycin can be used for that purpose.

Although, Tauxe et al.[11] used heart infusion agar containing 5% defibrinated rabbit blood to isolate *C. lari* from blood and stool specimens, Skirrow and Benjamin in 1980[1] reported the
isolation of C. lari from stool using selective agar containing vancomycin, polymyxin B and trimethoprim. On the other hand, Steel et al. used 5% sheep blood agar to isolate Campylobacter species including C. lari from stool, stressing the value of using non selective media, which permits the detection of unusual campylobacter species from human sources. Our results are in agreement with Steel et al. as our blood isolate grew on ordinary blood agar. However, isolation of this organism from stool was difficult on non-selective media. Fricker used a freshly prepared Preston media to recover C. lari. The same medium was also used by Holler to isolate C. lari and Campylobacter species from sewage system and waste water of sewage treatment plant. Glundt recommended the use of media containing 1.5% NaCl for the phenotypic differentiation of C. lari from other thermophilic Campylobacter species, while Nachamkin et al. used trypticase soy agar with 5% sheep blood for that purpose. He also recommended anaerobic atmosphere in the presence of trimethylamine N-oxide which is the most definitive test for C. lari identification. Other tests for identification included growth on 1.5% NaCl medium, susceptibility to triphenyltetrazolium chloride and resistance to nalidixic acid. Other authors reported nalidixic acid susceptibility and hippurate hydrolysis as the most important distinguishing tests between C. lari and C. jejuni. On the other hand, Magraud et al. recommended urease production for the identification of Campylobacter to the species level even for strains which are not of gastric origin. Therefore, for the isolation of C. lari from stool a selective medium is needed to inhibit other bacteria. A selective agar containing vancomycin, polymyxin B and trimethoprim can be successfully used as shown in our cases to isolate C. lari from stool. We recommend hippurate hydrolysis, susceptibility to nalidixic acid and cephalotin to differentiate C. lari from other related campylobacter species.

Conclusion We conclude from this report that C. lari is a distinct Campylobacter species that is emerging as an important pathogen in normal hosts as well as in immunocompromised adults and children. Microbiology laboratories should be aware of the methods of isolation and identification of C. lari from blood and stool of patients with bacteremia and enteritis.

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Collodion baby syndrome: the definitive management

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ABSTRACT
We report four cases of collodion baby managed by us in our Neonatal Intensive Care Unit in a two year period. This condition is stated to be rare, the precise incidence is not known. It may be frequent in this part of Saudi Arabia, due to consanguineous marriages. This hospital on average has 3000 deliveries per year. Early measures were taken to prevent dehydration, avoid infection and control temperature. Emollients in the form of propylene glycol in starch and vitamin A in zinc oxide cream were used successfully.

Keywords: Collodion, propylene glycol, zinc oxide.

This is a rare congenital problem and the mode of inheritance is autosomal recessive even in those cases where the skin becomes normal. The baby is encased in a shiny, brownish, yellow cellophane-like membrane and in most instances is premature. The membrane cracks with initial respiratory effort and desquamation takes place over several weeks. The complications in order of importance are:

1. Hypernatremic dehydration
2. Hypothermia
3. Infection

For future pregnancies prenatal diagnosis is possible by fetoscopy and fetal skin biopsy. Most of the cases progress to some form of ichthyosis. Five to ten percent develop a normal skin. A strict policy of management is essential if the child is to survive as was evident in our experience of four cases.

Case Reports

Case no. 1 This was a Saudi male child, born to a 16 year old primigravida at full term by normal vaginal delivery. He weighed 3 kg. Apgar was 9 at one minute. On examination he had abnormal skin over the whole body and ectropion. The appearance was typical of collodion baby. He was initially nursed in open cot. His progress was complicated on day 3 by hypernatremic dehydration, sodium 151 mmol/l (normal 135-145 mmol/l), raised urea 6.6 mmol/l (normal 1.8-6.5 mmol/l) and high creatinine 132 μmol/l (normal 40-70 μmol/l). This was corrected by increasing the volume of fluids given by intravenous and oral routes. By day 5 serum electrolytes were within normal limits. On day 6 he was febrile and blood culture grew Klebsiella. The septicemia was treated with intravenous ceftrixone (a third generation cephalosporin indicated by sensitivity), for a period of 10 days. The skin was treated with glycerine 50% in white soft paraffin and alpha keri oil. Pain was relieved by morphine. By day 5 his skin was desquamating and by two weeks it became erythematous. At the time of discharge the condition of the skin had improved but remained ichthyotic. He is now 2 years old and his skin is normal.

Case no. 2 This was a female Saudi child born at 34 weeks gestation by normal vaginal delivery. She had respiratory distress at birth requiring ventilatory assistance for 3 hours. Respiratory distress was probably due to abnormal skin covering around mouth and chest. On examination she had abnormal skin over whole body (Fig. 1) but mainly affecting face and trunk. She had eclabium and ectropion. The mother was 25 years old, had had 3 early miscarriages and had 1 other living child who was normal. This baby was nursed under radiant warmer and later transferred to an incubator with humidified air. Her serum electrolytes at 24-hours were abnormal sodium 150 mmol/l (normal 135-145 mmol/l), urea 7.2 mmol/l (normal 1.8-6.5) and creatinine 92 μmol/l (normal 40-70). Intravenous fluids were given...

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with rapid improvement and electrolytes returned to normal on day 4. This baby was initially nursed under radiant warmer because of ventilatory assistance required in the first 3 hours. Her skin was treated with intrasite gel. (propylene glycol in starch) mitosyl cream (Vitamin A in zinc oxide cream) and Baneocin, an antibiotic ointment for the flexures. Skin swabs were negative for culture. She was discharged home after a week on local treatment (Fig. 2). Review at 1 and 6 months showed her skin to be ichthyotic and requiring emollients.

Case no. 3 He was the younger brother of Case 1. He was born at term by normal vaginal delivery, weighing 2.7 kg. Apgar was 9 at 1 minute. On examination he had abnormal skin, mainly affecting face and trunk. He had eclabium, ectropion and crumpled ears (Figs. 3,4). Appearance was typical of collodion baby. Skin biopsy showed orthokeratosis with a thickened stratum corneum but no other abnormal findings. He was nursed in a humidified incubator in contrast with his brother, our first case. The skin was treated with intrasite gel and Mitosol cream. His course was uneventful and he was discharged on day 13 with an erythematous skin and mild desquamation. Follow-up in 1 month showed ichthyotic skin requiring emollients. Parents of Cases 1 and 3 were first degree cousins.

Case no. 4 A male Saudi child, breech presentation, was delivered by cesarean section at 34 weeks gestation. Apgar was 6 at one minute and 9 at five minutes. The mother was 24-years old and her 4 other children were well. Parents were first degree cousins. On examination the baby was covered with abnormal skin with eclabium and ectropion. This baby's skin was less severely affected compared to the other 3 cases (Fig. 5). Skin biopsy showed the same features as Case 3. From the start he was nursed in an incubator with humidified air and the skin was treated with intrasite gel. Skin swabs were negative on culture. Because of early treatment initiated with intravenous and oral fluids to prevent fluid loss this baby's electrolytes remained within normal limits. By 1 week of age the skin was desquamating and the baby was sent home on day 14 with a mildly erythematous skin (Fig. 6).

Discussion We have been fortunate in having to deal with 4 cases of Collodion Baby Syndrome over a relatively short period. This emphasized the need to adhere strictly to a policy of management, a fact which has not been stressed adequately to date. A recent case report by Buyse et al. emphasized the danger of transepidermal water loss, but the role of temperature regulation and infection control are also of major importance.

Case 1 was considered at first to be sufficiently well to be nursed in open cot and his skin responded reasonably to a mixture of 50% glycerine in starch. However, by the third day he was dehydrated and required intravenous fluids and subsequently became septiemic requiring antibiotics in the form of ceftriaxone for Klebsiella infection.

The 2nd case was salutary in as much as the infant had respiratory distress almost immediately due to the restriction on breathing imposed by the thickness of the collodion membrane around the chest and initially affecting the orifice of the mouth. To assist ventilation she was nursed under radiant warmer (air shield infant intensive care system) but as soon as possible was transferred to an incubator with humidification. However, her electrolytes at 24 hours were abnormal and IV fluids were given immediately with rapid and sustained improvement. Local treatment on this occasion was with propylene glycol in starch gel (intrasite). This preparation is sterile, can be warmed to a suitable temperature for comfortable application and is well tolerated. However, she also required an antibiotic locally to contain a clinically infected area, although skin swabs were reported negative on culture. Probably a combination of her prematurity and the need for nursing in open cot led to dehydration with an abnormal electrolyte pattern at 24 hours. Prematurity is a well recognized cause of dehydration. Intravenous fluids rapidly corrected the situation. By the 4th day her electrolytes were normal and she was discharged home after a further week on local treatment. When reviewed at 1 month and 6 months her skin was mildly ichthyotic and required emollients.

Case 3 was the brother of our first patient and was immediately placed in an incubator with humidification. Meticulous attention was given to temperature control. In addition to the sterile gel for local treatment vitamin A in zinc oxide cream (mitosol) was applied to those areas of skin which had desquamated and required additional protection. Because the vitamin A cream was more adherent it provided a better barrier than the gel. He progressed steadily and was discharged after 12 days with a mildly scaly erythematous skin. At follow up at 1 month the skin was generally ichthyotic. Skin biopsy taken on the second day showed only a thickened stratum corneum. This is a characteristic early finding and does not indicate the final outcome of the condition. Biopsy at 2 weeks may indicate this, and also whether the skin will become normal or ichthyotic.

Case 4 was the least problematical. Anticipation resulting in happy realization. Although the skin was less severely affected than the others it still showed all the classical features (Fig. 5). From the onset he was nursed in humidified air in the incubator. Temperature was closely controlled and any source of infection contained. He responded to the intrasite gel alone.
as the skin tended to peel off more easily rather than crack with resulting fissures and inflammation. We favor the use of this sterile hydrogel as it is presented in aluminum laminate sachets, which can be placed in hot water to warm before application. There was no evidence of irritation, no toxic systemic effects were evident in any of the 3 babies on whom it was used. However, it is imperative that any application to a large area of abnormal skin such as in collodion infants must not be capable of producing systemic toxic effects from absorption. In the collodion baby the abnormal skin causes increased fluid loss but may actually inhibit absorption.

Case 4 had no problem with dehydration, hypothermia or infection and was discharged home after 2 weeks with a slightly erythematous skin. At follow up he was mildly ichthyotic and erythematous.

Of these four collodion babies it is noteworthy that 3 were born prematurely, an accepted feature of the collodion baby syndrome. This, by itself, is a complicating factor as the needs of the premature infant further add to the problems produced by the collodion membrane. In 3 of the cases the parents were first cousins. Because the condition is rare elsewhere, it is unlikely that pediatricians will have formulated a policy of treatment that is sufficiently comprehensive to ensure the best possible outcome for the infant. Our experience with 4 neonates afflicted by this condition, all of whom survived but not without serious problems in the course of treatment in 2 of them, have convinced us that a strict policy of care is essential if these babies are to survive.

**Conclusion**

The following 5 points should be mandatory in a system of care:

1. All collodion babies should be transferred to a Neonatal Intensive Care Unit and nursed in an incubator immediately at birth.
2. Strict thermal and humidity control must be enforced until the collodion skin separates.
3. Infection must be anticipated and prevented.
4. Electrolytes should be monitored and dehydration anticipated.
5. Non toxic and, where possible, sterile emollients should be used on the skin as needed.

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