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Case Report Open Access

Melioidosis in Qatar: Case Series and Literature Review

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Abstract

Introduction: Melioidosis is a tropical infectious disease caused by Gram-negative bacteria *Burkholderia pseudomallei (B. pseudomallei)*. This soil-borne disease is endemic in Southeast Asia and Northern Australia.In our country it was reported once before in 2000 in a patient presented with subdural empyema.

Case Series Report: We are reporting four cases of Melioidosis presented to our hospital in very close time with different clinical presentations. All patients were from Indian subcontinent. 3 cases we treated with Meropenem plus Trimethoprim – Sulfamethaxazole followed by oral Trimethoprim - Sulfamethaxazole and Doxycycline for around 6 months with good clinical and radiological response, while the fourth case was treated with oral Trimethoprim - Sulfamethaxazole and Doxycycline but he lost follow up, there was no mortality reported in our case series for both types bactraemic and abactraemic Melioidosis.

Conclusions: This case series report highlights the importance of early identification of *B.pseudomallei* which requires a high index of clinical suspicion as well as good understanding of demographical and travel history. Microbiological identification of *B.pseudomallei* is essential and requires notification of the microbiologist for suspicion of that infection. Prolonged antimicrobial therapy is required for a better clinical outcome.

Keyword: Melioidosis;Bactraemic;Abactraemic Melioidosis;*Burkholderiapseudomallei* infection.

Introduction

Melioidosis is a tropical infectious disease caused by Gram-negative bacteria *B. pseudomallei*; it is widely distributed in the soil and water within endemic areas.

B. pseudomallei (the agent of Melioidosis) are related to the genus *Burkholderia* which includes another four species*: B. cepacia, B. gladioli, B. pickettii and B. mallei* [1, 2].

It is endemic in certain parts of the world including Southeast Asia and northern Australia [3].

Recent data indicate that it is now endemic to most of the Indian subcontinent, southern People's Republic of China, Hong Kong, Taiwan, Papua New Guinea, and other regions [4].

Qatar is a peninsula in Arabian Gulf with estimated population of 2 million in 2012, the number of economically active population doubled three times during seven years (from 444.133 in 2004 to 1.277,445 in 2011). This unprecedented growth resulted primarily from the recruitment of large numbers of foreign workers needed for the country's ambitious development plans. Most of this workforce is from South East Asia and Indian subcontinent [5].

Most cases reported in other regions were acquired during residence in or travel to disease-endemic regions. In our country it was reported once before [6].

We think that there is no local transmission of the disease and all cases are imported cases.

Melioidosis has different presentations including latent infection, local cutaneous lesions, sub-acute pneumonia, focal organ abscess, musculo-skeletal infection, and lethal fulminant pneumonia [3, 4, 7-10].

The disease can cause up to 20% of all community-acquired sepsis in the tropics, including 40% of sepsis-related mortality in Northern Thailand and up to ~20% in the higher-technology setting of Northern Australia [1,3,7,9,10].

First Case

47 year old Nepalese male, diabetic not on treatment working in Qatar for 2 years as Gardner with no recent travel history presented to our Accident and Emergency in Hamad Hospital on 23/9/2011 with10 days history of fever and burning micturation with no any other complain.

On examination patient looks dehydrated, drowsy and pale temp. 39.7 c ^{o}, Bp : 90/60, pulse:120/min .rep. 24 Systemic examination was unremarkable.

He was started on I.V Pipracillin- Tazobactam 4.5 grams IV every 8 Hours. His initial investigations showed leukocytosis 13.4 ×10^3/uL, hemoglobin 6.5 g/dl (required blood transfusion) with normal coagulation profile, normal renal function test, his liver enzymes where elevated (AST 56 U/L, ALT 49 U/L, ALP 626 U/L)

Blood culture were requested and initial results was showing gram negative bacilli reported later on as *B.pseudomallei*),

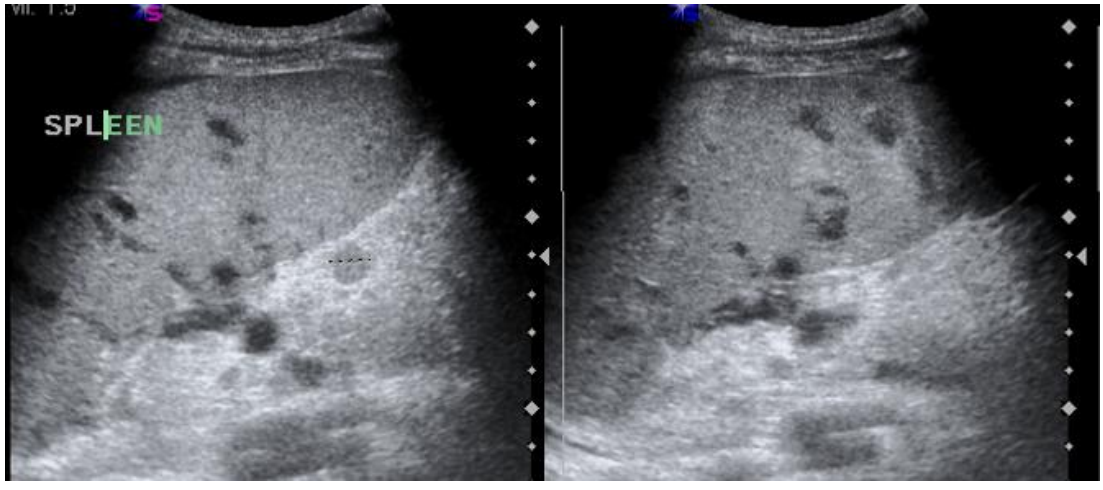
Antibiotics were changed to IV Meropenem 1 gram Q8Hrs; repeated blood culture on 28/9 was persistently positive for *B.pseudomallei*.

Ultrasound abdomen was requested which showed multiple hepatic and splenic lesions? Abscess (Photo 1), ultrasound guided drainage was done on 4/10 draining 70 ml of pus and pig tail catheter was inserted for three days. Repeated blood culture became negative.

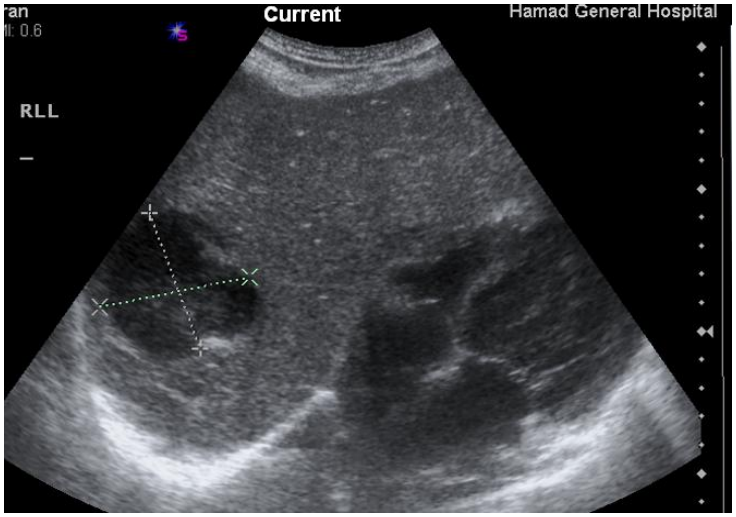
Patient received 15 days of I.V.Meropenem, and discharged on 12/10 on oral Trimethoprim – Sulfamethaxazole (TMP-SMX) double strength (DS) 960mg BID PLUS Doxycycline100 mg PO BID.

Followed in infectious disease outpatient clinic, repeated ultrasound abdomen on 26/12 showed no collection with complete resolution of the previously describe abscesses (Photo 2).Antibiotics were stopped a total of 100 days were received; follow up to one year doesn't show any evidence or recurrence.

Photo 1



Ultra sound examination of the abdomen shows multiple hypo -echoic lesions in the spleen suggestive of multiple splenic abscesses



Ultra sound examination of the abdomen show Complex well defined area in the right lobe of the liver measuring 9 x 409 c

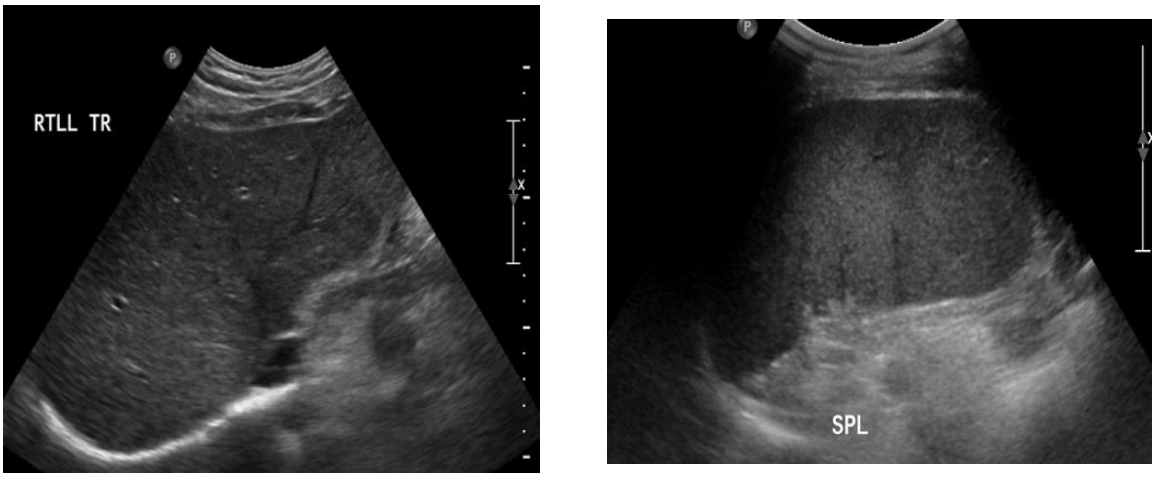


Photo 2: Ultra sound examination of the abdomen show normal appearance of the right lobe of the liver and spleen with no collection or abscess formation

Second Case

51 year old Indian male fisherman living in Qatar for the last 2 years with no recent travel history, known case of chronic carrier of hepatitis B virus with no regular follow up, occasional alcohol consumer, admitted on the 19/12/12 with 10 days history of fever and neck pain, he sought medical attention given oral antibiotics with no improvement.

On admission he was agitated, confused, febrile temperature was 38.2°C, Blood pressure was 100/60, and His systemic examination apart from neck stiffness was unremarkable.

He was diagnosed as Meningioencephalitis managed initially with I.V fluids, intravenous Ceftriaxone, Vancomycin and Acyclovir, admitted to intensive care unit. Laboratory results where within normal except for elevated liver enzymes ALT 90 U/L AST 194 U/L , high INR of 1.7 and high Procalcitonin level 25.14 ng/ml , C-reactive protein 293 mg/l ,ESR 58 mm/1hr , lumbar puncture was ordered but could not be done initially due to high INR,but it was done three days later and shows WBC 30 cells, mainly lymphocytes with high protein 5.12 g/l , glucose 3.5 mmol/l.

Blood cultures were requested on admission and reported as *B. pseudomallei*; antibiotics changed to Meropenem 1 gram IV Q 8 Hrs PLUS TMP-SMX 250mg of trimethoprim component IV Q6 Hrs according to patient weight.

Repeated blood cultured were negative, patient improved clinically, but unfortunately while he is on antibiotics he developed difficulty in walking, with signs of spinal card compression on clinical examination, urgent MRI lumbar spine was requested and showed Para vertebral collection 1.5 cm by 0.75 cm (Photo3). CT guided aspiration was done, pus was aspirated culture was negative for bacteria and tuberculosis. Meropenem PLUS TMP-SMX were continued, patient was transferred to rehabilitation unit, he showed good recovery where he was able to walk again without support, repeated MRI showed regression of the Para vertebral collection(Photo 4).

IV antibiotics were changed to PO Doxycycline plus TMP-SMX. He was treated for total six months. With no recurrence six months after completion of medical treatment.

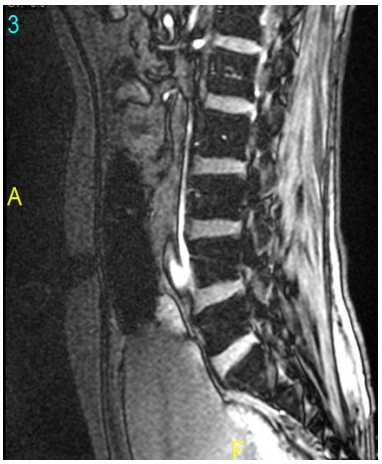


Photo 3: MRI lumbar spine shows Para vertebral collection 1.5 cm by 0.75 cm

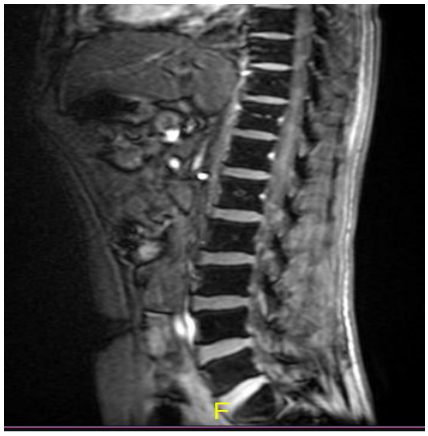


Photo 4: Follow up MRI lumbar spine showed regression of the Para vertebral collection

Third Case

36 year old Indian male patient living in Qatar for the past 4 year, he was working as fisherman. Newly discovered chronic carrier of hepatitis B virus He presented on 27/1/13 to our hospital with history of fever and right knee pain for the last 15 days, no history of trauma, raw milk ingestion, sexual contact, urinary symptoms or urethral discharge.

On examination the right knee was tender, swollen, hot with limitation of movement, no other joint involvement, admitted to surgical floor as right knee septic arthritis, started on IV Ceftriaxone 2 grams IV once daily.

His blood count and chemistry profile within normal, blood and urine culture where negative, fluid aspirate from the knee shows WBC -11300, mainly neutrophils.

Patient continued to have fever, MRI of left knee showed early osteomyelitis of lower one third of femur surrounded by tissue swelling and effusion (Photo 5), underwent incision and drainage of the knee joint multiple times, Synovial fluid and bone tissue culture showed *B.pseudomallei.*

Antibiotics were changed to Meropenem 1 gram IV Q 8 Hrs and TMP-SMX 200mg of trimethoprim component IV Q12 hrs according to patient weight which was given for 9 weeks which was changed to oral TMP-SMX plus Doxycycline upon discharge.

He was treated for total 5 months with good clinical improvement and no evidence of recurrence on 1 year follow up.

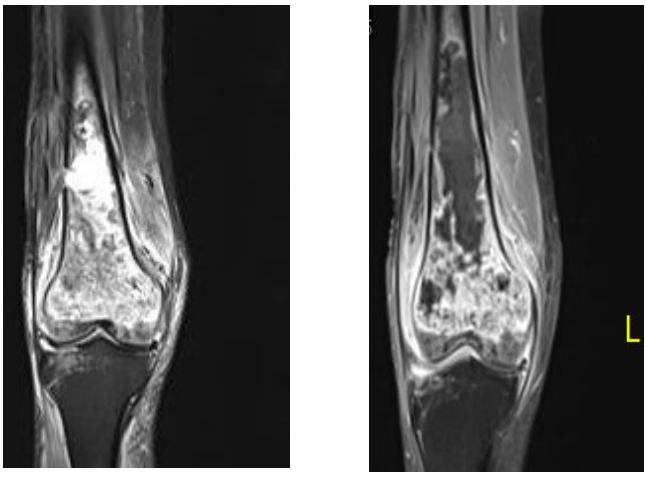


Photo 5: MRI of left knee shows early osteomyelitis of lower one third of femur surrounded by tissue swelling and effusion with intra medullary abscess formation

Fourth Case

20 year old Nepalese male, working in Qatar for 18 months as carpenter, He presented to our hospital on 10/6/12 with history of pus discharge from the right groin for 20 days (Photo 6), no history of fever,abdominal symptoms , trauma ,or sexual contact.

His complete blood count, chemistry and liver function within normal and urine, blood cultures where negative, but the swab culture shows *B. pseudomallei*. Ultrasound groin shows multiple lymph nodes with collection at subcutaneous tissue 7.7 ml of right groin area.

He refused hospital admission so he was given oral Doxycycline plus TMP-SMX.Planned for bone scan and MRI Pelvis to exclude osteomyelitis. Patient lost follow up. Summary of all cases reported in Qatar is shown in table 1.

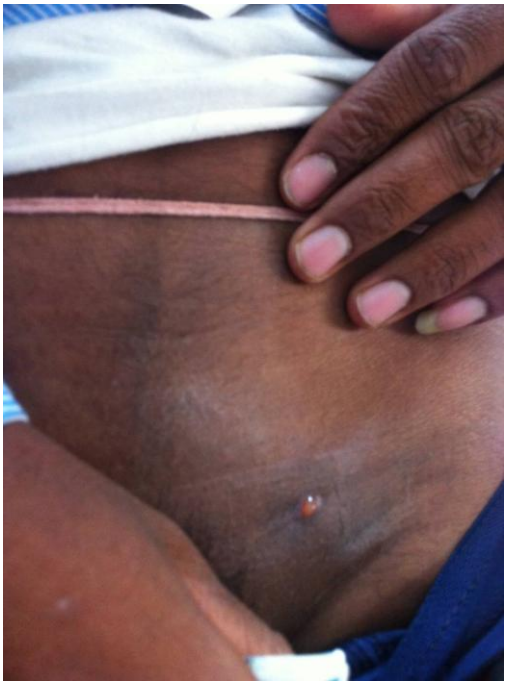


Photo 6: Right groin discharging sinus

Table 1: Summary of all cases of Melioidosis reported in Qatar

	Age	Nationality	Occupation	Length of stay in Qatar and travel history	Risk factors	Site of infection	Treatment	Duration	Outcome
1	47 yrs.	Nepal	Gardner	2 years with no recent travel history	Diabetes Mellitus	Bactraemia + liver and splenic abscesses	Iv Meropenem + TMP-SMX Followed by Doxycycline + TMP-SMX	3 months and 10 days	Cured
2	51 yrs.	India	Fisherman	2 years with no recent travel history	Chronic hepatitis B + alcohol consumption No History of Diabetes Mellitus	Bactraemia +vertebral osteomyelitis + paraspinal abscess	Iv Meropenem + TMP-SMX Followed by Doxycycline + TMP-SMX	6 months	Cured
3	36 yrs.	India	Fisherman	4 year with no recent travel history	Chronic hepatitis B, No History of Diabetes Mellitus	Knee septic arthritis + osteomyelitis	Iv Meropenem + TMP-SMX Followed by Doxycycline + TMP-SMX	6 months	Cured
4	20 yrs.	Nepal	Carpenter	18 months with no recent travel history	No risk factors	Groin sinus	Doxycycline + TMP-SMX PO	1 month	Lost follow up
5(Faraj S. etal.)	45 yrs.		Unknown	Returned from India few days prior to presentation	Diabetes Mellitus	Bactraemia + Disseminated infection	Ceftazidime + TMP-SMX followed by cefuroxime + TMP-SMX	6 months	Cured

Microbiology Identification

Laboratory identification of *B. Pseudomallei* can be difficult in our cases all identified by Vitek Compact (bioMérieux, Marcy l'Etoile, France) and Phoenix (Becton Dickinson, NewJersy and USA). Re-evaluation of the Gram stain and susceptibility pattern was done. The safety pin appearance of the GNB and resistance to Colistin and Gentamycin raised thepossibility of *B.pseudomallei* or *B. mallei*. The strain was sent to the Mayo Clinic Medical Laboratories (Rochester, USA) which identified the organism as *B.pseudomallei*by 16S RNAsequencing.2 strains genetic sequencing shows that they are different strains.

Discussion

B. pseudomallei and its role in human disease were first described by Whitmore and Krishnaswami in 1912 [11].Transmission of infection can occur through skin, lungs (inhalation, aspiration) andoccasionally by ingestion. Inhalation thought to be the most common route of acquisition of *B. pseudomallei* by different case reported in the literature [12, 13].

But now percutaneous inoculation during exposure to wet season soils or contaminated water is considered the predominant mode of transmission [14, 15, and 16].Cases of pneumonia following skin injuries are well documented, suggesting that the organism can reach the lungs via the hematogenous route [15].

Person-to-person transmission is extremely unusual, despite the large bacterial load in severely ill patients with Septicemic pulmonary Melioidosis [17, 18].Transmission from Mother to infant can happen during breastfeeding especially in the setting of *B. pseudomallei* mastitis [10, 19]. Laboratory-acquired infections and iatrogenic infections from contaminated hospital or surgical equipment occasionally occur [17, 20, and 21].

Transmission related to animal exposure is very rare; three possible cases have been described in Australia [22, 23]. Ingestion of water also postulated as uncommon routes of transmission. However, a study from Thailand raised the possibility that ingestion of water contaminated with *B.pseudomallei* may be a more common source of infection than previously thought, especially in endemic regions with unchlorinated water supplies [15, 17,24-26]. Sexual transmission is uncommon [27, 28].

The most important risk factors for Melioidosis are diabetes, hazardous alcohol use, and chronic renal disease [16, 29 - 32]. Other risk factors include chronic lung disease (present in 27 percent of cases in the Northern Territory Study) [33], thalassemia [31], and kava consumption [15] (The roots of the plant are used to produce a drink with sedative and anesthetic properties. Kava is consumed throughout the Pacific Ocean cultures of Polynesia, including Hawaii, Vanuatu, Melanesia and some parts of Micronesia). Malignancy, steroidand other immunosuppressive therapy, rheumatic heart disease and/or congestive cardiacfailure [30]. Pulmonary hemosiderosis [34], chronic granulomatous disease [35], and tuberculosis are probable risk factors, but are not yet confirmed to be independent risk factors [31].

In our case series risk factors which could be found Diabetes in 1 patients and chronic Hepatitis b infection in 2 patient one of them was also diabetic and alcohol consumer, one patient was healthy with no risk factors. Hepatitis B as a risk factor for Melioidosis was not previously described in the literature and presence of that relations need to be subjected tofurther studies.

Melioidosis can be classify to Acute disease is defined as symptoms lasting for less than two months. Chronic disease is defined as symptoms persisting for longer than two months [36].The incubation period following inoculating injury ranges from 1 to 21 days (mean nine days) [36, 37]and it can be as long as 26 years [38], depending on the inoculating dose, virulence properties of the isolate, mode of transmission, and host risk factors [39, 40] .Melioidosis is not an endemic disease in Qatar, all our cases are expatriates but since they had no recent travel history we think that they were incubating the disease prior to arrival to Qatar with relatively long incubation period.

Clinical presentation of Melioidosis can be variable but the most common manifestations are pneumonitis, lung abscess, soft-tissue infection, osteomyelitis, lymphadenitis, splenic abscess, liver abscess, and septicemia. As shown in our case series that bactraemic type with deep abscess formation is the most common presentation 75% of cases reported from Qatar (table 1).

Treatment of Melioidosis, even mild disease, should be with initial intensive therapy (at least
Two weeks of intravenous therapy) followed by eradication therapy orally for a minimum of three months. Initial intensive therapy with one of the following regimens Ceftazidime, Meropenem,Imipenem [41]. Trimethoprim-Sulfamethaxazole (TMP-SMX) may be added to other antibiotics aiming to decrease antibiotics resistance in specific clinical presentations such as neurologic, prostatic, bone, joint, cutaneous, and soft tissue Melioidosis [42, 43]. Further studies fail to show benefit from addition of trimethoprim-sulfamethaxazole in form of decreasing mortality or culture-confirmed recurrent Melioidosis [44, 45].

In eradication therapy Trimethoprim-Sulfamethaxazole is the drug of choice, combination of Doxycycline plus TMP-SMX was evaluated and studies does not show difference in the ratesof recurrence of Melioidosis but, a higher rate of adverse drug reactions were noticed when Doxycycline was added to regimen [46].

Other drugs were evaluated for treatment of Melioidosis like Amoxicillin-Clavulanate alone and oral Quinolones alone or in combination with Azithromycin and found to be lesseffective in preventing relapse than eradication therapy with TMP-SMX and Doxycycline with or without Chloramphenicol [47-51].

All of our patients were treated initially with either Ceftazidime or Meropenem followed byoral antibiotics including Doxycycline / TMP-SMX for 3-6 months except for one patient wholost his follow up.

Our patients who were treated with combination therapy showed good clinical response and drugs were well tolerated which may suggest that patients may get benefit from combination therapy but of course our number of patients was small and bigger studies are needed to evaluate this issue. Relapse after apparent cure of has been reported and may reach up to 15% per year of follow-up [41]. In our cases no relapse was documented with follow up 6-12 months.

Conclusion

Melioidosis, although rare in this geographic region, should be considered in the differential diagnosis for ill residents or travelers from areas of endemicity. Confirmed human sporadic cases in the Middle East have been reported in Iran, and suspected cases in Egypt, the United Arab Emirates and Saudi Arabia has been reported but not confirmed [54] and one confirmed case In Qatar, Cases in animals have also been reported from Iran, Saudi Arabia, United Arab Emirates [55, 56].

All our reported cases are from expatriates namely from India and Nepal we believe that those cases are imported but further evidence for the existence of *B. pseudomallei* as epizootic or in soil is laking in our region and further studies needed. We are reporting series of confirmed case diagnosed in Qatar in very close period of time and this is considered the first confirmed series of cases in humans diagnosed in our region, we could not find a clear link between those cases neither in demographic characteristics nor in genetic sequencing for two of those cases. Our cases had different clinical presentations ranging from mild infection to severe Septicemic type all treated medically with appropriate surgical intervention when needed with good outcome and no mortality recorded in our cases. Two of our cases found to be chronic carriers of hepatitis B infection and we think that further studies are needed to determine if it could be a significant risk factor for the disease.

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