



# Non-healing Wounds: A Delayed Wound Infection by Mycobacterium Tuberculosis

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## Abstract

**Introduction** Non-healing wound causes significant morbidity and mortality of patients. One of the rare causes behind non-healing wound infection is *M. tuberculosis* which often remains undiagnosed.

**Aim** The aim of this study was to determine the tuberculosis as one of the causes of non-healing wound.

**Methods** Wounds that did not heal even after secondary suturing and tissue biopsies were sent for histopathological examination. The cases diagnosed with tuberculosis received anti-tubercular treatment. Follow-up was done after 7 and 14 days of treatment, and response was seen in terms of reduction in inflammation and discharge.

**Results** Of the 36 patients, five patients had tubercular infection out of which one patient revealed tubercular granuloma, two revealed epitheloid cells, Langhans cells, whereas two revealed non-specific chronic inflammation in histopathology.

**Conclusion** A high degree of suspicion and tissue biopsy is required in case of delayed or non-healing wounds to diagnose tuberculosis as a cause. Even if typical tubercular granuloma is not visible in histopathology, the presence of epitheloid cells, giant cells, Langhans cells or predominant lymphocytic infiltrate equally suggests tubercular tissue infection.

**Keywords** Non-healing wound · Tubercular granuloma · Epitheloid cells · Langhans cells and wound tuberculosis

## Introduction

Non-healing wounds remain a major cause of morbidity in post-operative patients mostly owing to anaemia, obesity and immune compromised state. Lack of suspicion and difficulty in diagnosis of wound tuberculosis adds in increasing the morbidity by further delaying the wound healing. This occurs mostly due to reactivation of latent tuberculosis that is defined as a state of persistent immune response to mycobacterium tuberculosis antigens, which is harbouring

as a primary focus somewhere else in the body, with no evidence of clinically manifest active TB [1]. Tuberculosis is an ancient disease and has been described in the earliest literature: Rig Veda and Atharva Veda as YAKSHMA, but unfortunately it is still not a disease of the past. As per the Global TB Report 2017, the estimated incidence of TB in INDIA was approximately 28,00,000 accounting for about a quarter of the world's TB cases [2]. Latent *M. tuberculosis* infections present one of the major obstacles in gaining complete remission of tuberculosis. The aim of this study was to determine the tuberculosis as one of the causes of non-healing wound.

## Materials and Methods

**Type of Study:** Prospective observational study

**Place of Study:** Department of Obstetrics and Gynaecology, M.L.N. Medical College, Prayagraj, UP

**Duration of Study:** 12 months (August 2018–July 2019)

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**Sampling Method:** Incidental sampling

**Sample Size:** 36 patients, divided in two groups depending upon evidence of wound tuberculosis in wound biopsies.

Case group-: Cases with evidence of wound tuberculosis in tissue histopathology;  $n = 5$  (13.88%).

Control group: Cases without evidence of tubercular infection in tissue histopathology;  $n = 31$  (86.11%).

**Inclusion Criteria:** Non-healing surgical site wounds

**Exclusion Criteria**

1. Known cases of tuberculosis
2. Known cases of HIV
3. Known cases of skin disorder

**Procedure** Patients operated for LSCS or abdominal hysterectomies with non-healed wounds even after secondary suturing were included in this study. Pus/discharge from wounds was sent for culture and sensitivity. All related investigations like CBC and blood sugar estimations were done. Tissue biopsies from the margins of the wound were sent for histopathological examination. The presence of tubercular granuloma and/or epithelioid cells/giant cells/Langhans cells and/or predominant lymphocyte infiltrates was taken as positive findings to diagnose wound tuberculosis.

**Assessment Parameter** Response to anti-tubercular treatment in terms of reduction in inflammation and discharge on day 7 and day 14 and beyond.

**Results (Table 1)**

Most of the study population belonged to 20–40 years of age, had low parity and were from rural background and of lower middle/lower classes. The BMI of most of the patients was normal to overweight (18.6–29.99). All the demographic variables in both the groups were comparable (Table 2). Most of the patients had serosanguinous discharge, and rest had purulent discharge; however, the difference was statistically nonsignificant, but the presence of pain was much less in the case group with statistically significant difference ( $P$  value  $< .05$ ).

Bacteriological study of wound discharge was more or less negative (80%) in the case group but positive in the control group (58%). However, the difference was again statistically nonsignificant. In both the groups, anaemia was the most commonly associated co-morbidity (80%; 90.32%) followed by obesity with no significant difference (Table 3).

The patients had varied presentations, but the ultimate outcome was little or no sign of improvement with traditional antibiotics and regular dressing (Table 4). All patients had no positive contact history with tuberculosis patients. Histopathologically, typical tubercular granuloma was found in only one patient (20%); predominant chronic inflammatory infiltrates, lymphocytes without giant cells or epithelioid cells were there in two patients (40%); the presence of epithelioid cells and giant cells was there in two patients (40%) (Table 5). Healing process was earliest (within 7 days) most commonly evidenced by reduction of discharge (60%) and subsidence of inflammation took a little longer (more than 7 days) in most of the patients (60%) (Table 6).

**Discussion**

Non-healing post-operative wound significantly increases the morbidity of the patients putting them under financial, psychological as well as social stress. It also spoils the reputation and peace of the treating obstetrician–gynaecologist. Though the majority of non-healing wound cases were middle-aged (20–40 years), from rural background and of low socio-economic status, the nonsignificant difference in case and control group states that any of the patients presenting with non-healing wound may have wound tuberculosis even in the absence of active tuberculosis somewhere else in her body as has also been shown by Kiazzyk et al. [3]

Most of the times, the bacteriological study of the wound discharges was negative and we considered this negativity as the result of antibiotics the patients were already having. This is a proven fact that bacteriological cultures of the body secretions in patients on antibiotics are usually negative as shown by Perveen et al. [4]. High positivity rates of wound tuberculosis in culture negative patients in this study emphasise on having suspicion of wound tubercular infections in patients with negative bacteriological culture, that too more if pain is either nil or mild.

Abdominal wound healing is related to the general condition of the patient as well as the abdominal obesity as also described by Pierpont et al. [5]. The presence of anaemia, obesity and diabetes definitely adversely affects the wound healing; the nonsignificant difference in the presence of these co-morbidities in case and control groups shows that these factors per se do not increase the chance of wound tuberculosis and hence advocates the suspicion of tubercular wound infection in all the patients with delayed wound healing and recommends sending tissue biopsies to confirm the diagnoses. The same recommendations have also made by Mazid et al. [6].

Since we excluded the patients who were on anti-tubercular treatment as well as none of our patients had clinical symptoms of tuberculosis, the occurrence of wound

**Table 1** Distributions of patients and their demographic variables

Total No. of patients	Cases with evidence of tubercular infection in tissue histopathology (case group) No. (%)	Cases without tubercular infection (control group) No. (%)	
36	5 (13.88%)	31 (86.11%)	
Demographic variables	Case group (n=5) No. (%)	Control group (n=31) No. (%)	P value
Age (in years)			
< 20	1 (20%)	4 (12.9%)	0.89
20–40	3 (60%)	19 (61.29%)	
> 40	1 (20%)	8 (25.80%)	
Parity			
P1–2	3 (60%)	14 (45.16%)	0.968
P3–4	2 (40%)	12 (38.70%)	
≥ P5	0	5 (16.12%)	
Residential area			
Urban	1 (20%)	12 (38.70%)	0.41
Rural	4 (80%)	19 (61.29%)	
Socio-economic status			
Upper class	0	1 (3.22%)	0.781
Upper middle class	0	2 (6.41%)	
Lower middle class	3 (60%)	13 (41.93%)	
Lower class	2 (40%)	15 (48.38%)	
Body mass index			
< 18.5	0	4 (12.90%)	0.55
18.6–24.99	2 (40%)	10 (32.25%)	
25–29.99	2 (40%)	16 (51.61%)	
> 30	1 (20%)	1 (3.22%)	

**Table 2** Character of wound discharge and associated pain

	Case group (n=5){13.88%}	Control group (n=31){86.11%}	P value
Wound discharge			
Serosanguinous	4(80%)	29 (93.54%)	0.30
Purulent	1((20%)	2 (6.45%)	
Associated pain			
Present	1 (20%)	28 (90.32%)	0.002
Absent	4 (80%)	3 (9.67%)	

**Table 3** Bacteriological study of wound discharge

	Case group (n=5){13.88%}	Control group (n=31){86.11%}	P value
<i>E. coli</i>	0	9(29.03%)	0.746
<i>Staphylococcus aureus</i>	1(20%)	5(16.12%)	
<i>Pseudomonas</i>	0	3(9.67%)	
<i>Klebsiella</i>	0	1(3.22%)	
No growth	4(80%)	13(41.93%)	

**Table 4** Associated co-morbidities

Co-morbid conditions	Case group (n=5){13.88%}	Control group (n=31){86.11%}	P value
Diabetes	1(20%)	3(9.67%)	0.51
Anaemia	4(80%)	28(90.32%)	
Obesity	2((40%)	5(16.12%)	

tuberculosis might be due to reactivation of latent tubercular focus at primary sites. India being a very high prevalent country with tuberculosis, more so in Uttar Pradesh (India TB Report 2019) [7], we all carry a dormant focus in our bodies that tends to reactivate whenever the immunity falls. Trauma or surgery additionally raises the chances of infection causing local vascular derangements and altered tissue vitality. It has been estimated that 5–10% of latent infections reactivate and cause active tuberculosis when patients health gets compromised (WHO) (Figs. 1, 2)

Histopathological presence of tubercular granuloma definitely confirms the diagnosis, but mere presence of even scarcely placed Langhans giant cells, Langhans cells,

epitheloid cells and predominant presence of lymphocytes equally suggests tubercular wound infection in areas of high prevalence like ours.

Here, we wish to acknowledge that all the patients who were started with anti-tubercular treatment were reported to the institutional department of TB/chest in accordance with government order by Department of Health and Family Welfare in 2018.

## Conclusion and Recommendation

Delayed wound healing is worrisome as well as traumatic for both surgeons and patients. This is one of the common presentation of infection by *M. tuberculosis* which is lesser suspected than their prevalence especially in high endemic

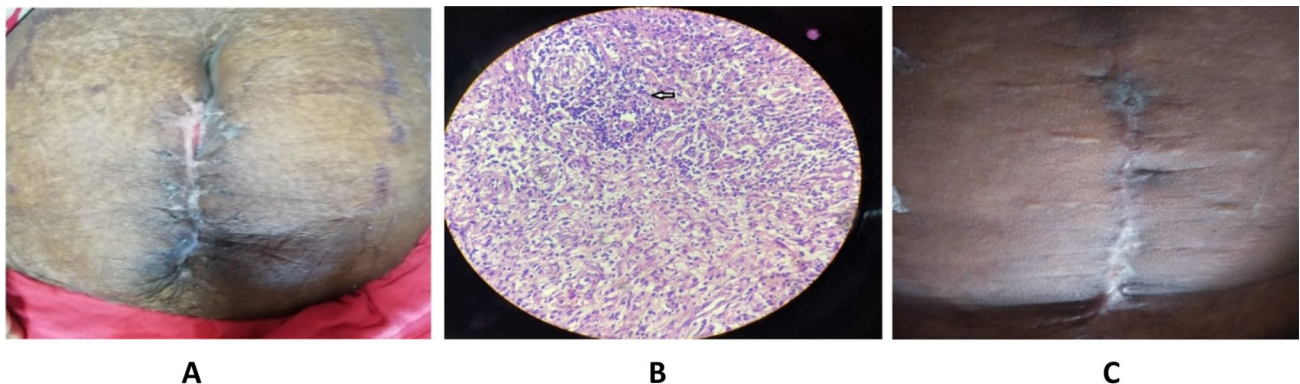
area. This study recommends having high degree of suspicion of wound tuberculosis and sending wound biopsies in all the patients with delayed/non-healing at earliest. Since sending just a bit of the tissue from the wound for histopathology will not put additional stress on the patient, missing the diagnosis will definitely go on increasing her morbidities with ongoing dressings and stress of having an open wound over her abdomen that is not healing. We should not depend exclusively on the presence of typical tubercular granuloma for diagnosis; the presence of giant cells/Langhans cells and predominately chronic lymphocytic infiltrates equally suggests tubercular infection.

**Table 5** Details of the case group showing evidence of tubercular infection in wound biopsy (n=5)

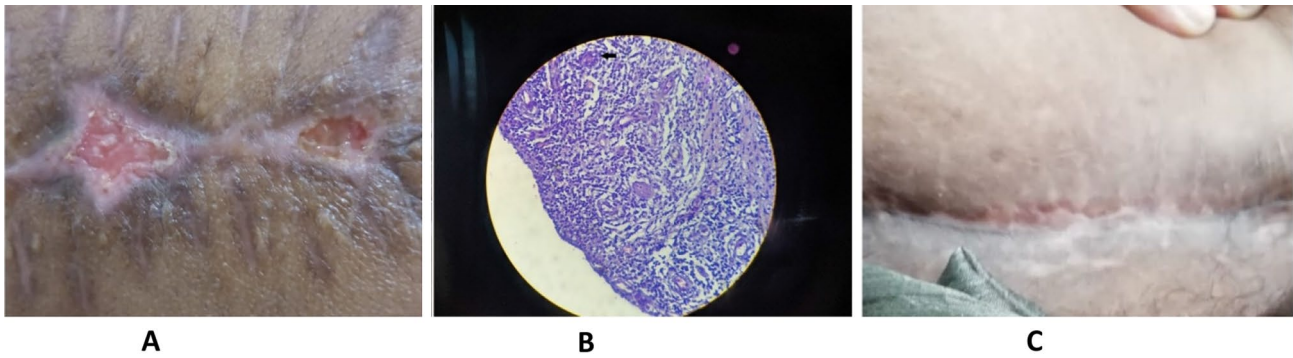
Cases	Clinical presentation	Time interval	Procedure	Time of Detection	Histopathological finding
1.	Discharging sinus	50th post-operative day	LSCS	60 days	Dense chronic inflammation predominantly lymphocytes with granulation tissue
2.	Stitch line abscess	14th post-operative day	LSCS	21 days	Scattered epitheloid cells and macrophages
3.	Non-healing wound	18th post-operative day	Abdominal hysterectomy	35 days	Epitheloid cells, granuloma, giant cells
4.	Non-healing ulcer	30th post-operative day	Abdominal hysterectomy	46 days	Focal area of giant cells
5.	Non-healing wound	20th post-operative day	LSCS	30 days	Dense inflammatory infiltrate of lymphocytes, neutrophils and plasma cells

**Table 6** Post-treatment response and relieve in symptoms in cases (n=5){13.88%}

Follow-up response	Less than 7 days		7–14 days		More than 14 days	
	No.	%	No.	%	No.	%
Reduction in discharge	03	60%	01	20%	01	20%
Reduction in inflammation	02	40%	02	40%	01	20%



**Fig. 1** **a** Female 25 years presenting with abdominal wound discharging sinus; **b** photomicrograph showing scattered epitheloid cells with dense inflammatory infiltrate with lymphocytes; **c** post-treatment healed wound after 2 months



**Fig. 2** **a** Female 32 years presenting with post-operative non-healing ulcerated abdominal wound; **b** photomicrograph showing subepithelial zone of epithelioid cells with dense inflammatory infiltrate of lymphocytes, neutrophils; **c** post-treatment healed wound after 4 months

### Compliance with Ethical Standards

**Conflict of interest** We certify that we have no affiliation with or involvement in any organisation or entity with any financial interest (such as honoraria, educational grants, participation in speakers) or non-financial interest (such as personal or professional relationship, affiliation, knowledge) in the subject matter or material discussed.

**Informed Consent for Human Studies** All procedures followed were in accordance with ethical standard of responsible committee on human experimentation (institutional and national) and with Helsinki Declaration of 1975, as revised in 2008. Informed consent was obtained from all patients for being included in the study.

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