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Review

Tuberculosis before and after the Black Death (1346–1353 CE) in the Hospital of St John the Evangelist in Cambridge, England

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ABSTRACT

This research explores how the prevalence of tuberculosis (TB) in a medieval hospital was affected by the demographic and social changes that following the Black Death (1346–1353 CE), the initial years of the Second Plague Pandemic. To do this, skeletal remains of individuals buried at the Hospital of St John the Evangelist in Cambridge, England, that could be dated to living before (n = 77) or after (n = 55) the Black Death were assessed for evidence of TB (indicated by destructive lesions of the spine, ribs, large joints, and other recognised criteria). Overall, the odds of females having skeletal lesions caused by TB were over four times higher than males. No significant difference was detected in the prevalence rates in those who lived before and after the Black Death (7.8%, 6/77 before and 11.0%, 6/55 after). However, the odds of females having skeletal evidence of TB were over five times greater after the Black Death than they were before. These findings indicate that women may have been 1) more susceptible to TB, 2) surviving longer post-infection than men, and/or 3) that women with TB were more likely to be admitted to the Hospital especially following the Black Death. It is also possible that impairment due to TB infection may have been a contributing factor for entry into the Hospital for women but not men.

1. Introduction

To date, there have been three major plague pandemics (caused by the bacterium *Yersinia pestis)*: the First Plague Pandemic (541 – 767 CE), the Second Plague Pandemic (1346 –c. 1690 CE), and the Third Plague Pandemic (1894–c. 1940 CE) [1]. The Second Plague Pandemic was one of the most devastating pandemics in global history [1,2]. It is believed that this outbreak originated in China [1,3,4] and then swept through Southeast Asia in the early 1300s' before spreading across the Middle East and into Europe in 1346 [5]. The initial years of the Second Plague Pandemic were marked by a catastrophic mortality rate: this period would later come to be known as the Black Death (1346–1353 CE) [1]. It has been estimated that between 30 and 65 percent of the population of Eurasia died during this period [1].

The demographic, social, and economic consequences of the Second Plague Pandemic have been extensively explored [1,2,6–8]. Yet, few studies have explored temporal trends in other infectious diseases (besides *Y. pestis*) and how such diseases impacted societies during this turbulent period in history. Though limited to conditions that affect the skeletal system, osteoarchaeological studies are able to contribute key insights about past health and individual experiences. Through the analysis of human skeletal remains this paper aims to explore how the prevalence of tuberculosis (TB), caused by one of the species of the *Mycobacterium tuberculosis* complex (MTC), was affected by the demographic and social changes following the Black Death. To explore this, we assessed human skeletal remains of individuals from Cambridge, England who could be dated to living before the plague arrived in the region in 1349 CE, and those that lived after this time.

1.1. Background: Medieval Cambridge

By the thirteenth century, Cambridge was an economically thriving

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mid-sized market town with a recently founded university and a population of about 2500–4000 [9,10]. The economy was largely based on agriculture and trade that was facilitated by the river. As such, the majority of the towns inhabitants were laborers who were involved either directly, or indirectly in agricultural activities [11–13]. Immediately prior to the outbreak of the plague in Cambridge in 1349 CE, the population had risen to around 5800 inhabitants [9]. Unfortunately, no textual records exist that detail the overall impact of the Black Death on the population of Cambridge, though it can be assumed that Cambridge experienced a similar fatality rate to the rest of England (between 40 and 60%). If this was indeed the case, the number of fatalities would be between around 2300–3500 individuals [14].

2. Materials & methods

2.1. Materials: the Hospital of St. John the Evangelist

As part of the 'After the Plague: Health and History in Medieval Cambridge' (ATP) project, human skeletal remains of individuals buried at the Hospital of St John the Evangelist were analysed. The Hospital was a charitable religious institution established *c.* 1195 to provide pastoral and spiritual care, but not medical care as we know it, for the poor and infirm [15]. It was dissolved to create St. John's College in 1511 [15]. The Hospital acquired burial rights between c. 1204–15 CE and documentary and archaeological evidence indicates that the cemetery was in use *c.* 1204/1214–1467/1511 CE [16]. The cemetery associated with the Hospital was excavated during 2010–11 by the Cambridge Archaeological Unit. This excavation unearthed 400 complete and partial in situ burials [16]. The individuals buried in the cemetery were predominately inmates who died whilst in residence at the Hospital, in addition to a smaller number of townspeople, benefactors and 'corrodians', who were wealthy elderly lay people who paid to live a religious institution for the rest of their lives [17]. This assemblage consists primarily of adult individuals, with relatively few individuals under the age of 18 years [16].

2.1.1. Osteological methods

Each skeleton was assigned a 'project skeleton number' (PSN) that served as a unique identifier for the ATP project. Individuals are referred to by these numbers throughout. The human skeletal remains in this study were fully assessed following accepted professional guidelines [18,19]. Individuals that were over 25% complete that had vertebrae and ribs and that could be dated to having died prior to, or after the Black Death were included in this analysis (n = 132). Lesions were described, and a differential diagnosis undertaken for each individual. Diagnostic imaging which included plain X-rays and/or microCT scans were acquired where necessary to aid in the process of differential diagnosis.

Within this work, the term 'adult' is used to describe an individual that was over 18 years of age at the time of their death. The term 'preadult' is used to refer to an individual that was less than 18 years of age at the time of their death. The biological sex of each adult skeleton was estimated by examining the sexually dimorphic characteristics of the pelvis and skull [18,20,21]. Genetic sex for selected adult (n = 43) and preadult individuals (n = 11) was determined using aDNA analysis [22,23]. In cases where the pelvis and skull were damaged and thus unable to be assessed, or were absent, and in cases where the DNA was not preserved, biological sex was classed as unobservable. Within this work, the terms 'female' and 'male' are used to denote biological sex estimates derived through osteological/genetic methods, while the terms 'women' and 'men' are used to discuss the experiences of individuals based on these biological sex estimates in order to better contextualise the social implications of these findings.

Age-at-death of adult individuals was estimated based on the degenerative changes observable on the pubic symphysis [24], auricular surface [25], sternal rib ends [26,27] and the sternal end of the clavicle [28]. Age-at-death for preadult individuals was estimated using dental formation or epiphyseal fusion (if teeth were not present) [29–31]. No individuals under the age of 7 years of age met the inclusion criteria for this study. Individuals were divided into the following age categories: late child (LC) (7–12 years), adolescent (ADO) (13–17 years), young adult (YA) (18–25 years), young middle adult (YMA) (26–35 years), old middle adult (OMA) (36–44 years), mature adult (MA) (46–59 years), old adult (OA) (60+ years). If age-at-death could not be determined due to incompleteness or damage, individuals with complete epiphyseal fusion were classified as 'adult' (18 years +).

2.1.2. Dating methods

An extensive program of radiocarbon dating was undertaken and a date range was assigned to each skeleton based on their stratigraphic location within the burial sequence. In addition to standard calibration, allowance has been made for various factors that can affect radiocarbon determinations on human bone making them appear older than the date an individual died and that are not covered by standard calibration (marine dietary offset, bone turnover during life). See Cessford and Alexander for full methodological description [32].

2.1.3. Diagnostic approach & criteria used to identify tuberculosis

A threshold approach which employed weighted diagnostic criteria (as recommended by Refs. [33,34]) was combined with traditional differential diagnosis. The pathogenesis of TB depends on the size of the inoculum, the virulence of the organism and the immune response of the host [35]. The disease progression may lead to tuberculosis meningitis, organ TB or miliary TB, where multiple tubercles are present throughout the involved tissues. The skeletal system can be affected as the result of direct infection or through hematogenous spread of the disease. As such, any skeletal elements can be affected, though the most common skeletal elements affected are the vertebrae, tarsals and metatarsals, carpals and metacarpals, and the ribs [35]. The weighted diagnostic criteria, derived from clinical and palaeopathological studies, as well as a list of the diseases/causes considered for each lesion can be found in Table 1. Pott's spine, also called tuberculous spondylitis or spinal TB, is clinically considered pathognomonic for TB [35] and was considered 'strongly diagnostic' within this research. Lesions that have been identified in clinical or paleopathological studies that have a strong association with TB, but are not pathognomonic, were considered 'diagnostic'. 'Suggestive' lesions include those that are typical of TB, but can also occur as the result of several other conditions (for additional information about this approach see Refs. [33,34]). One strongly diagnostic lesion or two diagnostic lesions were necessary for a case to be considered probable. A case was considered possible if one diagnostic lesion was observed as well as one or more suggestive lesion.

2.1.4. Statistical methods

Odds ratios (OR) were calculated in order to explore differences between groups. ORs measures the probability (or odds) of an event occurring in one group compared with another group [59]. ORs are a widely used epidemiological tool that is well suited to compare diseases prevalence between skeletal samples including those with non-normal distributions [60,61] The standard error and 95% confidence intervals were calculated according to Altman [59]. Statistical significance was set at $P \leq 0.05$.

3. Results

Skeletal evidence of TB was identified in 9.1% (12/132) of the individuals examined (Table 2 and 3) (Figs. 1 and 2). A higher frequency of preadults (<18 years of age at the time of their death) (4/30; 13.3%) had skeletal evidence of TB than did adults (defined as over 18 years of age at the time of their death) (8/102; 7.8%), but this was not statistically significant (OR = 1.81; 95% CI = 0.5 to 6.5, p = 0.36). In adult individuals, a higher frequency of females (6/40; 15.0%) had skeletal

Table 1
Threshold diagnostic criteria for tuberculosis. SD = strongly diagnostic lesions: sign considered pathognomonic for the disease; D = diagnostic lesions: clinically diagnostic or well-established lesions for diagnosis in paleopathological literature; S = suggestive lesions: lesions that are consistent with but not diagnostic of the disease.

	Pathology	Diagnostic strength	Differential diagnosis	Reference
1	Pott's diseases (tuberculous spondylitis, spinal TB): osteolytic destruction of one or more vertebral body and the intervertebral disk space(s) resulting in vertebral collapse and subsequent gibbus formation	SD	Spondylitis caused by pyogenic, granulomatous, fungal or parasitic agents, neoplasms	[[35]: 330–331] [36–39]
2	Substantial osteolytic lesion(s) on the anterior aspect of the vertebral body with minimal evidence of reactive bone formation	D	Same as above (1)	[37] [[38]: 231] [[35]: 332] [40,41]
3	Osteolytic destruction on the os coxae and/or sacrum	D	Neoplasms, osteomyelitis	[[35]: 329–330] [[38]: 239] [[40]: 985]
4	Reactive new bone formation on the os coxae, sacrum, and/or anterior aspect of proximal femora (signs of an overlying cold abscess)	D	Neoplasms	[35] [[38]:239] [[40]:985] [[41]: 329–330]
5	Circumscribed osteolytic lesion(s) that affect the frontal bone, parietal bone(s), and/or the maxilla (especially at the junction of the zygoma, primarily in preadults)	D	Neoplasms, mycosis, Langerhans cell histiocytosis	[[38]: 248–253] [[42]:156–157] [[40]:1345–1348] [43]
6	Tuberculosis dactylitis (spina ventosa): concentric expansion of the metacarpals, metatarsals, and/or phalanges (predominantly in preadults)	D	Osteomyelitis, syphilitic dactylitis, fungal dactylitis, sarcoidosis, brucellosis, hyperparathyroidism, leukemia, spondyloarthropathies (psoriatic arthritis, reactive arthritis)	[[35]: 339] [[38]: 242] [[42]: 162]
7	Tuberculosis arthritis of the hip that may involve the destruction of femoral head/neck and/or acetabulum, with possible ankylosis	D	Septic arthritis, osteoarthritis, psoriatic arthritis, rheumatoid arthritis, trauma	[[35]: 323–325 modified from Ref. [44]: 333–337] [[38]: 235–239] [45,46]
8	Focal osteolytic lesions at growth plates and metaphases of the knee, elbow, ankle wrist (in preadults)	D	Septic arthritis, psoriatic arthritis, juvenile rheumatoid arthritis	[[35]: 342–343] [42]
9	Osteolytic lesion(s) on the visceral/costal surfaces of the ribs and/or sternum	D	Neoplasms; pulmonary sarcoidosis	[[35]: 345] [47–51]
10	Cortical expansion of the ribs: substantial remodeled new bone on the visceral surface that results in enlargement of shaft (assessed radiographically)	D	Chronic pleural infections including pneumonia, Paget's disease	[48] [[52]: 925]
11	Focal destruction of subchondral surfaces and/or tuberculosis arthritis of the shoulder, wrist, ankle, metacarpal and metatarsal joints	D	Septic arthritis, osteoarthritis, psoriatic arthritis, rheumatoid arthritis	[[35]: 323–325, modified from Ref. [44]] [46]
12	Diffuse subperiosteal new bone formation on the visceral surfaces of multiple ribs (isolated to head, neck and shaft)	S	Chronic respiratory diseases that cause pleural inflammation (pneumonia, actinomycosis, bronchitis, emphysema, pleurisy etc.), lung cancer, poor air quality	[[35]: 323–325, 343–344] [47–51] [[52]: 925] [53]
13	Focal osteolytic lesions affecting one or more vertebra with substantial reactive bone formation, or those that affect the neural arch	S	Neoplasms, brucellosis, osteomyelitis	[[38]: 230]
14	Diffuse, symmetrical periosteal new bone formation on the diaphysis of long bones (hypertrophic osteoarthropathy secondary to TB)	S	Pachydermoperiostosis, chronic venous insufficiency, and a range of cardiopulmonary, gastrointestinal, endocrine, haematological, and inflammatory conditions.	[49,54–57]
15	Subperiosteal new bone formation on endocranial surface	S	Various infections, intracranial hemorrhage, hydrocephalus	[42,58]

Table 2
Demographic distribution of individuals with skeletal evidence that is diagnostic or strongly diagnostic of skeletal tuberculosis from the detached burial ground of the Hospital of St John the Evangelist, Cambridge, England.

Age Category	Age Range (in years)	Male		Female		Unobs.		Total		Total
		Pre	Post	Pre	Post	Pre	Post	Pre	Post	
Late child (LC)	7–12	0/4	0/3	0/2	0/1	1/8	0/1	1/14	0/5	**1/19**
Adolescent (ADO)	13–17	0/1	1/3	1/1	1/1	0/4	0/1	1/6	2/5	**3/11**
Young Adult (YA)	18–25	1/6	0/5	0/6	2/4	0/2	0/1	1/14	2/10	**3/24**
Young Middle Adult (YMA)	26–35	1/2	0/4	0/4	1/1	0/1	–	1/7	1/5	**2/12**
Old Middle Adult (OMA)	36–45	0/5	0/6	1/6	0/3	–	–	1/11	0/9	**1/20**
Mature Adult (MA)	46–59	0/9	0/11	0/6	1/2	0/1	–	0/16	1/13	**1/29**
Old Adult (OA)	60+	0/4	0/4	0/2	0/2	–	–	0/6	0/6	**0/12**
Adult (A)	18+	–	–	1/3	0/1	–	0/1	1/3	0/2	**1/5**
Total		**2/31**	**1/36**	**3/30**	**5/15**	**1/16**	**0/4**	**6/77**	**6/55**	**12/132**

evidence of TB than did males (2/56; 3.6%). Though not statistically significant, the odds of adult females buried in the Hospital burial ground having skeletal evidence of TB was 4.8 times that of adult males (OR = 4.8; 95% confidence interval [CI] = .91 to 25.0; p = 0.06).

Evidence of TB was found 7.8% (6/77) of those that lived and died prior to the Black Death (1349 in Cambridge), and in 10.9% (6/55) of those that lived afterwards. No significant difference was detected in prevalence rates between these groups (OR= 1.45; 95% CI = 0.44 to 4.76, p = 0.54). However, a higher frequency of adult females that lived in the post-Black Death period had TB (4/13; 30.8%) than did adult females that lived before (2/27; 7.4%). The odds of adult females who lived after the Black Death developing skeletal evidence of TB was 5.6 times of those adult females that lived before (OR = 5.6; 95% CI = .86 to 35.7; p = 0.07).

Table 3
Skeletal lesions likely caused by TB observed on each individual from the detached burial ground of the Hospital of St John the Evangelist, Cambridge, England. Numbers correspond to the descriptions of lesions provided in Table 1. X = present, 0 = absent, - = unobservable.

PSN	Sex	Age Category	Pre/post 1349	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
25	M	ADO	Post	X	0	0	0	–	0	–	0	X	0	0	X	0	0	–
28	F[a]	ADO	Post	0	X	0	0	X	0	0	0	0	0	0	0	X	0	0
47	F[a]	MA	Post	X	0	0	0	–	0	0	–	X	0	0	X	X	0	–
70	F[a]	ADO	Pre	0	0	0	X	–	0	X	–	0	X	0	X	0	0	–
75	F[a]	A	Pre	0	X	X	0	–	0	0	–	X	0	X	X	0	0	–
88	F[a]	YA	Post	0	X	0	X	0	0	X	–	0	0	0	X	X	X	0
90	F[a]	YA	Post	X	X	0	X	0	0	X	–	0	0	0	X	0	0	0
190	M	YMA	Pre	0	X	0	0	–	–	0	–	0	0	0	X	0	0	–
239	M[a]	YA	Pre	0	0	X	0	0	0	0	–	X	X	0	0	0	0	0
252	F	OMA	Pre	0	X	X	X	–	–	0	–	X	0	0	X	0	0	–
339	F[a]	YMA	Post	0	X	0	X	0	0	0	–	X	X	0	X	0	0	0
374	U	LC	Pre	0	X	X	X	–	0	0	0	0	0	0	0	0	0	–

[a] Indicates that biological sex confirmed/determined though aDNA analysis [22,23].

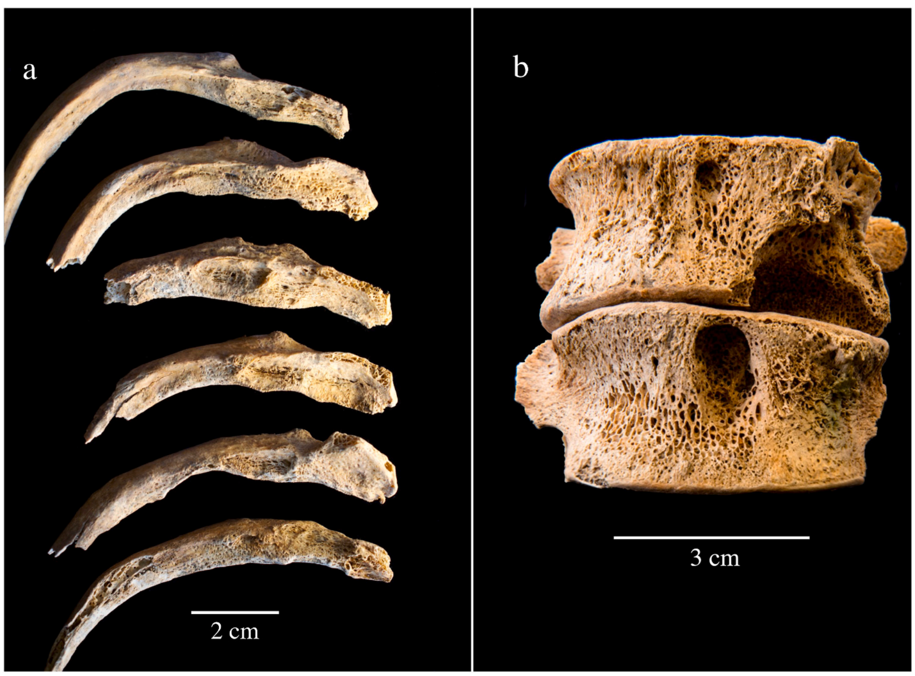

Fig. 1. a) Subperiosteal new bone formation on the visceral surfaces of the right ribs of an adult female (PSN 339) that lived after the Black Death and b) lumbar vertebrae with destructive and proliferative lesions caused by tuberculosis in an adult individual (PSN 190) that lived prior to the Black Death. Both individuals were buried at the Hospital of St John the Evangelist, Cambridge, England.

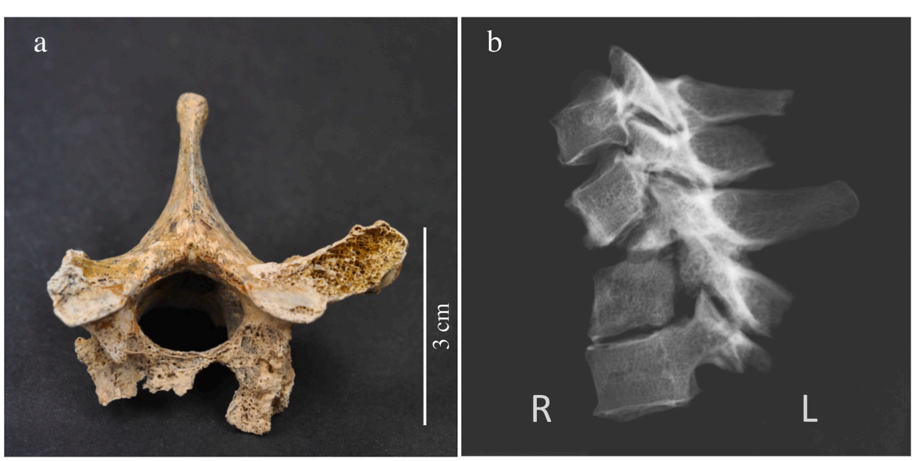

Fig. 2. a) Superior view of second thoracic vertebra and b) plain X-ray (lateral view) showing the destruction of the second thoracic vertebral body (Pott's spine) of an adult female (PSN 90) that lived after the Black Death plague pandemic who was buried at the Hospital of St John the Evangelist, Cambridge, England.

4. Discussion

This study shows strong continuity in the frequency of skeletal TB over time, rather than the decrease predicted to coincide with the drastic reduction in the population caused by the Black Death. This is not overly surprising. Although it is possible that diet, housing and/or clothing may have improved, as historians have often hypothesized, such changes would be specific to particular sectors of the population [7,8]. The people considered here are the middle to poorer end of town-dwelling craftspeople and laborers and may not have benefited from improvements affecting (for instance) rural agricultural workers. For those living in towns, living conditions remained much the same throughout the Late Medieval period; for instance, both before and after plague, poorer people tended to live in small, often crowded dwellings [10–12].

The observed difference between the sexes with skeletal evidence of TB requires more discussion. Adult females were more likely to have skeletal manifestations of TB than their male counterparts overall, as well as in both the pre- and post-Black Death groups. This could indicate that women were more likely to contract TB; for example, they may have spent more time in crowded settings, or indoors caring for members of their households and the community more generally. Another possibility is that men and women were equally likely to have contracted TB, but the disease was more likely to manifest skeletally in women. This, however, is unsupported by modern clinical research that shows that skeletal TB has an equal incidence between the sexes [62,63], even though men typically have higher prevalence rates of TB than women [64–67]. Rather than a difference in the presentation of the diseases, it is possible that women survived longer post-infection than did men who may have succumbed before skeletal lesions could manifest.

Another factor to consider is the demographics of the individuals buried at the Hospital. Though the Hospital largely served individuals selected as recipients of charity according to specific Late Medieval criteria of need and merit, there were several other ways that individuals came to reside in the Hospital or be interred in its burial ground [17]. As such, a small number of corrodians and university scholars who resided in the Hospital were likely also included in this sample, as well as a small number of comparatively wealthy benefactors. This being the case, the findings of this study likely reflect both the health of the underlying population and the imposed selection criteria for hospital entry and burial.

Like most medieval hospitals, the Hospital of St. John had limited capacity and only a selected few of Cambridge's poor that were deemed 'worthy' were able to be accommodated [17]. It has been estimated that the Hospital in Cambridge had 10 beds, with a maximum capacity of 20 individuals at any given time [68]. Once admitted, inmates and corrodians would generally spend the remainder of their lives within the Hospital. As such, lengthy periods of time (possibly years), could pass before space became available. When space was available, inmates were likely selected from many potential candidates through a largely subjective process [17]. In light of the finding of this study, it is possible that the physical impairment due to chronic illness played a role in perceptions of worthiness to receiving Christian charity specifically for women.

The more than five-fold increase in the odds of women having skeletal evidence of TB after the Black Death may represent an increase in chronically ill women within Cambridge. This could indicate that women were more susceptible to TB following the Black Death, that they were more likely to develop skeletal lesions, or that women with TB were more likely to be admitted to the Hospital. The latter may be evidence of a shift in the admission criteria for the Hospital that reflected larger societal trends and concerns regarding infectious disease following the Black Death. Later medieval charity placed an increasing emphasis upon the demonstrable moral worthiness of the recipients, with strictures against giving charity to the able-bodied: Incapacity to work due to severe long-term illness such as TB may have formed one criterion [69]. These findings highlight the need for additional research into the underlying social and environmental conditions that affected the chronic health burden in medieval towns and how this impacted medieval communities.

Evidence of skeletal TB was less commonly observed in preadult individuals within this sample. This could reflect a true difference in the prevalence rates between adults and preadults from the medieval period, though it is also possible that the observed disparity could be due to difficulties in identifying and diagnosing TB in preadult remains [42]. Furthermore, the Hospital sample contained relatively few preadults, with no individuals under the age of five recovered [16]. As preadults were much less likely to be admitted to the Hospital, it is not possible to determine if there were true differences in the prevalence of TB between adults and preadults.

4.1. Limitations

As with every archaeological study, there are several limitations that impact our ability to generalise these findings. Firstly, TB only affects the skeletal system in a small percentage of those infected. Jaffe reports skeletal involvement in 3–5% of untreated individuals [40]. Today, though similar percentages have been reported in recent clinical studies [63], it is widely accepted that skeletal manifestations occur in 1–3% of modern cases [70]. Thus, as with all palaeopathological studies, it is not possible to determine the true prevalence rates of TB within this sample, though the true prevalence rate of TB in this population must have been significantly higher than the skeletal data here indicate. A further limitation is that the individuals included in this study represent only a subset of medieval Cambridge; those interred in the burial ground of a charitable institution for the poor. As such, these results are likely not reflective of Cambridge society as a whole. Conversely, this means that they may be able to provide information on how people understood illness and used it as a criterion for categorizing people (for instance, as worthy of receiving charity). The trends identified within this work suggests that there may be underlying social and/or environmental factors that may have caused more women (in comparison to men) who were chronically ill with TB to be present in medieval Cambridge and be housed within the Hospital following the Black death. Future study comparing this sample to others from other contemporary contexts may shed further light on the social reasons behind this trend.

5. Conclusions

These findings suggest that TB remained a consistent feature of the disease landscape in medieval Cambridge, even after the drastic reduction in the population that followed the Black Death. Overall more females had skeletal evidence of TB than males which suggests that they may have been; 1) more susceptible to developing skeletal lesions associated with TB, or 2) that females infected with TB survived longer and were thus more likely to develop skeletal lesions. The over five-fold increase in the odds of females who were buried in the Hospital with skeletal evidence of TB after the Black Death suggests that: 1) females may have been more likely to contract TB following the Black Death, and/or that 2) impairment due to TB infection may have been a contributing factor for entry into the Hospital for women but not men. As the presence of disease in past populations was affected by numerous factors, many of which were not uniformly experienced by members of society, further research is required in order to explore the factors that may have contributed to skeletal evidence of an increased infection rate of TB in women.

Author contribution

JD: Collected data: palaeopathology, conceived and designed the analysis, performed analysis, wrote paper SAI: Collected data: osteology, database management CC: Excavated archaeological site, provided archaeological and historical background, collected and analysed data: undertook archaeological dating programme PDM: Analysed data, funding acquisition, project oversite JER: Analysed data, funding acquisition, project oversite All authors provided critical feedback and helped shape the research, analysis and manuscript.

Declaration of competing interest

None.

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Transparency declaration

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