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Leprosy: The age-old companion of humans – Re-evaluation and comparative analysis of Avar-period cases with Hansen's disease from the Danube-Tisza Interfluve, Hungary

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ABSTRACT

In recent years, our knowledge of leprosy in the past has substantially been enriched. Nonetheless, much still remains to be discovered, especially in regions and periods from where no written sources are available. To fill in some research gaps, we provide the comparative analysis of eight Avar-period leprosy cases from the Danube-Tisza Interfluve (Hungary). In every case, to reconstruct the biological consequences of leprosy, the detected bony changes were linked with palaeopathological and modern medical information. To reconstruct the social consequences of being affected by leprosy, conceptualisation of the examined individuals' treatment in death was conducted. In every case, the disease resulted in deformation and disfigurement of the involved anatomical areas (rhinomaxillary region, feet, and/or hands) with difficulties in conducting certain physical activities. These would have been disadvantageous for the examined individuals and limited or changed their possibilities to participate in social situations. The most severe cases would have required continuous support from others to survive. Our findings indicate that, despite their very visible disease and associated debility, the examined communities did not segregate leprosy sufferers but provided and cared for them, and maintained a strong enough social network that made their survival possible even after becoming incapable of self-sufficiency.

1. Introduction

1.1. Leprosy, a stigmatised disease today

Leprosy, also known as Hansen's disease (HD), is a chronic granulomatous infection that mainly affects humans [1–3]. It can be propagated by one of two acid-fast, rod-shaped bacterial species, the long well-known *Mycobacterium leprae*, sometimes called Hansen's bacillus, and the more recently discovered *Mycobacterium lepromatosis* [1, 3–6]. Both pathogens are aerobic, non-motile, non-spore-forming, obligate intracellular bacilli that cannot be cultivated *ex vivo* but must be grown in animal models, chiefly nine-banded armadillos (*Dasypus*

Abbreviations: Hansen's disease, HD; Tuberculoid leprosy, TT; Lepromatous leprosy, LL; Borderline tuberculoid, BT; Borderline borderline, BB; Borderline lepromatous, BL; Multidrug therapy, MDT; Rhinomaxillary syndrome, RMS.

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novemcinctus) and mice (*Mus musculus*) [3,7–10].

The mechanisms by which leprosy bacilli spread from one person to another is still a matter of debate [1,3,11,12]. Expulsion and consequent inhalation of contaminated droplets/aerosols, usually from the nose but also the mouth of an infected individual, is thought to be the main route of human-to-human transmission [3,4,12–14]. People having prolonged close contact with an individual who has untreated leprosy are considered at greater risk of contracting HD [3,15–17]. Fortunately, only a small proportion of people exposed to leprosy bacilli (~5%) are successfully infected, of whom only about 20% go on to develop clinically active disease, as up to 95% of the world's population is naturally immune to HD [12,15,17,18]. Leprosy bacilli multiply very slowly; and thus, it may take a long time after infection – around 5 years on average but sometimes up to 20 years or even more – before the first signs and symptoms of the disease become apparent [1,5,13,14,19]. After this asymptomatic incubation period, HD generally progresses slowly, and may present a broad spectrum of clinical manifestations, strongly correlating with the patient's immune response to leprosy bacilli at the time of infection and during the course of disease [1,4,5,16,20].

Patients mounting strong cellular responses, accompanied by a deficit of humoral responses, develop tuberculoid leprosy (TT) that is a localised, minimally contagious, paucibacillary form with a less severe disease course and a tendency to self-healing [1,4,7,10,21]. On the other hand, patients with predominant humoral responses and poor cellular responses represent lepromatous leprosy (LL) that is a systemic, highly contagious, multibacillary form with a more severe disease course and without spontaneous regression/resolution [1,4,7,10,21]. Between these two immunologically stable, polar types of the spectrum (TT and LL), there are the three unstable, borderline forms of HD: borderline tuberculoid (BT), borderline borderline (BB), and borderline lepromatous (BL) [1,22]. The vast majority of leprosy patients fall into borderline types, with a gradual decrease in cellular responses and a gradual increase in humoral responses from BT through BB to BL [21,23–26]. Eventually, the transient, borderline forms of HD may progress to one of the polar types (TT or LL) [1,22,26].

Leprosy bacilli have a low optimal growth temperature of around 30 °C and a tropism for cells of the reticuloendothelial system (e.g., macrophages) and peripheral nervous system (e.g., Schwann cells) [1,2,5,8,10]. These would explain that HD primarily affects the cooler, superficial areas of the human body, such as the nasal mucosa, the skin (particularly over the face and extremities), and the peripheral nerves (especially within and close to the skin) [1,5,8,20]. Over time, other parts of the human body, including the skeleton, can also become involved in leprosy [27–30]. Dermatological, neurological, and orthopaedic complications of HD may potentially lead to irreversible changes in the patient's physical appearance and mobility [15,29,31–33].

Early, accurate diagnosis and prompt, adequate treatment are of paramount importance to prevent or at least minimise visible physical disfigurement (especially in the face, hands, and feet) and temporary or persistent physical impairments [5,12,27,29,34]. In four decades since the global implementation of the highly effective and well-tolerated multidrug therapy (MDT), millions of former HD patients have successfully completed it; and hereby, been considered to be cured of leprosy [35–37]. Nonetheless, while MDT can cure the disease by eradicating leprosy bacilli from the patient's body, it cannot reverse already existing physical deformities or disabilities; in fact, leprosy reactions (i.e., intermittent and recurring inflammatory episodes triggered by the body's immune response against alive or dead leprosy bacilli) that can occur not only prior but during or after completion of MDT, if unrecognised, left untreated or improperly managed, may produce further damage [38–43]. Unfortunately, among those individuals considered to be cured by MDT, there are a large number, who still experience physical sequelae of the disease, e.g., deformities or disabilities, that have an adverse effect on their ability to carry out normal day-to-day activities [32,37,39,44].

Religious and social meanings associated with leprosy or the changes in the patient's physical appearance and mobility that result from it may generate stigmatising attitudes toward and negative beliefs about people affected by the disease [32,45]. Leprosy-related stigma is a strong barrier to health-seeking behaviour, engagement in care, and adherence to treatment, which leads to worsening of the disease; and thus, contributes to maintaining the vicious cycle of stigmatisation [35,46,47]. Besides physical disfigurement and impairments, social stigma and discrimination may predispose HD patients to experience psychological (e.g., anxiety and depression), economic (e.g., income loss and unemployment), and social (e.g., restrictions in social participation) problems that also can negatively affect their quality of life [44,48–50].

1.2. Leprosy and the stigma related to it in the past

Leprosy-related stigma is not a modern phenomenon but thought to be as old as leprosy itself that is an ancient scourge afflicting humans since millennia [45,51–54]. Nonetheless, it is important to note that our knowledge and understanding of how society viewed HD and treated its victims in the past is changing, due in part to the study of leprosy in the Middle Ages becoming a lively field of research in recent years [55,56]. However, most of these studies focus their attention on Europe during the High Middle Ages (11th–13th centuries CE) or Later Middle Ages (14th–15th centuries CE) as the result of the large number of written sources dealing with HD. As most of these written sources were created in Christian environments, our understanding of leprosy is heavily influenced by religious, Christian authors and communities, while less attention has been given to other geographical regions or cultural contexts. The predominant earlier view was that in mediaeval Christian Europe, HD was perceived to be either a physical manifestation of immorality or evidence of divine punishment of the victim, and that people with the disease were uniformly stigmatised, compulsorily segregated from the healthy society, and forced to live in leprosaria (i.e., hospitals established to care for sufferers of HD) because of their supposed sinfulness [54,55,57–59]. However, most of the stereotypical ideas held today about how leprosy was viewed and its victims were treated in the Middle Ages of Europe seem to have been to a large extent constructed in the 19th century CE [55,60]. In fact, the contemporary perceptions and reactions of mediaeval Christian society to HD and people with the disease seem to have been more complex and often contradictory, ranging from revulsion to admiration [55,61,62]. Recent research into leprosy in the Middle Ages pointed towards ways in which HD was not only viewed as a sign of sin but also interpreted as a sign of divine favour: leprosy sufferers were believed to endure soul-cleansing purgatory on earth; and thus, would be permitted to pass straight to heaven after death [55,57,60,63,64]. Even when separated spatially by their residence in a leprosarium, they were far from being cut off from the healthy society, and were objects of compassion and understanding of their plight, because they were thought to be closer to God than other people [55,65,66].

Although collaboration between researchers from different disciplines, from history to bioarchaeology, already has substantially enriched our knowledge and understanding of HD in the Middle Ages of Europe, much still remains to be discovered [55]. In recent years, new sources of information – namely the results of palaeopathology and palaeogenomics – changed the possibilities of research, as these new sources provide possibilities to fill in the gaps left by the written sources, but also to study the perception of leprosy in geographical regions and archaeological periods where written sources are scarce or not available at all, especially the centuries between the Late Roman period and the High Middle Ages (5th–10th centuries CE). One of the main aims of palaeopathology, a key contributor to the field of bioarchaeology, is to explore the disease experience in the past, which necessarily encompasses the examination of the social perception of disease in the archaeological period in question (e.g., mediaeval period), including stigma and discrimination [66,67]. This is because an individual's disease experience is related not only to the signs, symptoms, and

complications of the disease they are afflicted with, but to the social perceptions and reactions to that particular disease (e.g., leprosy) [66,68]. The study of disease-associated stigma in the past often is limited to the investigation of mortuary treatment, chiefly manner of burial and place of burial, of individuals displaying skeletal evidence of disease [66]. Consequently, studies attempting to link mortuary treatment to disease-associated stigma can deal with only those medical conditions that may affect the skeleton and leave bony changes characteristic enough to establish a definitive diagnosis [66].

Although leprosy is one of those diseases that can leave readily identifiable bony changes on skeletonised or mummified human remains, predominantly in the rhinomaxillary region of the face, the small bones of the hands and feet, and the long tubular bones of the lower legs, there are some major difficulties in diagnosing the disease in past populations [56,69,70]. 1) Even if HD was present in an individual at the time of death, it may not be evident in their skeleton, as they did not live sufficiently long with leprosy for bony changes to develop [66,67,71]. 2) Even if the course of HD was long enough to allow characteristic skeletal lesions to occur before death, the ability to notice these alterations is to a high degree dependent on the completeness and preservation of the skeleton in question [71,72]. And 3) even if characteristic bony changes can be detected in the examined human remains, they cannot be considered as pathognomonic features of leprosy, as other pathological conditions or even taphonomic processes can cause the same or similar lesions; and thus, only the specific distribution pattern of alterations in the human skeleton can provide a definitive diagnosis of HD [69–73]. Consequently, the investigation of mortuary treatment as related to leprosy and potential leprosy-related stigma is limited to individual cases exhibiting that specific distribution pattern of bony changes [66]. It is important to bear in mind that the mortuary treatment does not necessarily reflect the prevailing attitude of mediaeval society toward people with leprosy, as it appears that whatever stigma may have existed, and however the afflicted were treated in life, there are numerous instances of people with HD being treated no differently in death than other deceased in the Middle Ages of Europe [66,74].

1.3. Aims

During the Early Middle Ages, the Inner Asian Avars, arriving from the Eurasian Steppe together with other Eastern European nomadic people, conquered and united the Carpathian Basin under a single political rule, and established the Avar Khaganate in 567/568 CE [75–77]. The Avar Khaganate, ruled by a khagan, lasted almost a quarter of millennium, and remained a regional political power in Eastern and Central Europe until its collapse, due to external attacks and internal power struggles, in the first third of the 9th century CE [75,76,78]. In the Danube-Tisza Interfluve, the concentration of burials lavishly furnished with gold- and silver-decorated weapons and belts, various insignias, and valuable prestige objects, indicating the prominent social position of their owner, suggests that the Avar power centre lay in this region [77,79]. It was proposed that the successive westward migration of the Avars in multiple waves into the Carpathian Basin led to the separate introduction or re-transmission of different *Mycobacterium leprae* strains into Eastern and Central Europe, including Hungary; and thus, contributed to the spread of leprosy in this geographical region during the early mediaeval period [80–82]. Based on written sources and the spatial distribution of Mediterranean and Merowingian artefact types, we can assume that there was a persistent long-range mobility during the first century of the Avar period, which could have also affected the spread of infectious diseases, including HD [83–85].

Although internal written sources from the Avar Khaganate did not survive or maybe never even existed, there is a detailed archaeological record left behind. Its study can contribute to expanding and improving our knowledge and understanding of not only leprosy, but also the disease experience by both those afflicted with HD and society at large during the early mediaeval period, when treatment was not an option for the victims; and thus, the disease could have developed in its natural course, eventually leading to severe physical disfigurement and impairments. The aim of our paper is to provide a comparative analysis of leprosy cases from the core territory of the Avar Khaganate, the Danube-Tisza Interfluve. Most of the Avar-period cases in question have been only briefly summarised in previous papers by Marcsik and her colleagues [86,87], with no implication to the biological and/or social consequences of the disease. To reconstruct the type and biological consequences of HD, the detected macroscopic bony changes were linked with palaeopathological and modern medical information. Furthermore, to reconstruct the social consequences of being affected by leprosy in the Avar-period Danube-Tisza Interfluve, conceptualisation of the examined individuals' treatment in death was conducted. Besides re-evaluation of the already published cases, a newly discovered HD case is also demonstrated. Our study gives us a unique insight into the biological consequences of living with leprosy and illustrates the social attitude toward its victims in early mediaeval Hungary.

2. Materials and methods

2.1. Materials

From the Avar-period Danube-Tisza Interfluve, only 12 probable cases with leprosy have been published up to now – seven cases (**KD21**, **KD41**, **KD119**, **KD271**, **KD517**, **KD518**, and **KD520**) from the Kiskundorozsma–Daruhalom-dűlő II site [86,88], two cases (**KK61** and **KK245**) from the Kiskundorozsma–Kettőshatár I site [86,89], one case (**KK706**) from the Kiskundorozsma–Kettőshatár II site [86], and two cases (**HC?** and **HC81**) from the Hajós–Cifrahegy site [87]. From these 12 cases, only seven (**KD41**, **KD119**, **KD271**, **KD518**, **KD520**, **KK61**, and **HC81**) have been included in the present study, as in the five other cases, the macroscopic bony changes observed during the re-evaluation of the skeletons were not sufficiently conclusive to establish the definitive diagnosis of HD (**KD21**, **KK245**, and **KK706**), the skull was not available for the macromorphological re-evaluation (**KD517**), or the skeleton could not be linked to a particular grave, which precluded the conceptualisation of this individual's treatment in death (**HC?**). In addition to the seven already published cases, a newly discovered probable case with leprosy from the Sükösd–Ságod site (**SS214**) is also demonstrated in the current paper (Tables 1–3 and Supplementary figures 1–8).

All of the aforementioned archaeological sites belong to the same larger geographical region, the Danube-Tisza Interfluve, but form two tight clusters (Fig. 1). At Kiskundorozsma, three Avar-period cemeteries have been excavated, but only two of them (Daruhalom-dűlő II and Kettőshatár I) contained individuals with a definitive diagnosis of HD. These two sites are located in the close proximity of the Tisza River (Fig. 1), on opposite sides of the Maty Creek (Daruhalom-dűlő II to the west, whereas Kettőshatár I to the east), separated only by about 200 m [90–95]. The smaller Kiskundorozsma–Daruhalom-dűlő II cemetery with 93 burials (Fig. 2a and Supplementary text 1) was abandoned during the last third of the 7th century CE, whereas the larger Kiskundorozsma–Kettőshatár I cemetery with 298 burials (Fig. 2b and Supplementary text 2) is dated to the 8th–9th centuries CE [92,93,95–97]. Based on the archaeological chronology, the Kiskundorozsma–Kettőshatár I site was established right after the abandonment of the Kiskundorozsma–Daruhalom-dűlő II site, and it has been suggested that it was used by the same community that relocated to the other side of the Maty Creek [90,91,93–95,97]. There is a third, smaller Avar-period cemetery (Kiskundorozsma–Kettőshatár II) with 43 burials, which was located right next to the Kiskundorozsma–Kettőshatár I site, but this cemetery is not discussed in detail in the current paper, because the only leprosy case (**KK706**) published from here have been excluded following the re-evaluation of the skeleton, as the observed bony changes were not sufficiently conclusive to establish the definitive diagnosis of HD.

Table 1
Burial features (location, construction, dimensions, and orientation of the grave, positioning of the corpse in the grave, and grave goods placed along with the deceased) of KD41, KD119, KD271, KD518, KD520, KK61, HC81, and SS214.

Case IDs & References	BURIAL FEATURES						
	Location of the grave	Grave construction	Dimensions of the grave	Orientation of the grave	Positioning of the corpse	Grave goods	Other
KD41 [95]	• within the cemetery boundaries (Fig. 2a)	• rectangular with rounded corners, vertical walls, and an even bottom; • ledges; • posthole structure (Supplementary figure 1a)	• length: 2.26 m; • width: 1.34 m; • depth: 0.95 m	• north-west to south-east (340°–160°) (Supplementary Fig. 1a and b)	• extended supine; • head to the north-west; • feet to the south-east; • arms placed at the sides; •legs alongside each other (knees touching) (Supplementary Fig. 1a and b)	• iron knife; • iron buckle; • copper-alloy earring; • copper-alloy belt buckle; • copper-alloy belt mounts; • copper-alloy belt end; • flint stone; •domestic sheep and chicken bones (Supplementary figure 1b)	• an iron object, and textile and ceramic vessel remains in the filling of the grave
KD119 [95]	• within the cemetery boundaries (Fig. 2a)	• rectangular with rounded corners, vertical walls, and an even bottom; • coffin; • bed burial? (Supplementary Fig. 2a and b)	• length: 2.21 m; • width: 1.10 m; • depth: 0.72 m	•north-west to south-east (340°–160°) (Supplementary Fig. 2a and b)	• extended supine; •head to the north-west (tilted to the right); • feet to the south-east; • arms placed at the sides; •legs alongside each other (knees touching) (Supplementary Fig. 2a and b)	•domestic sheep bones (Supplementary figure 2b)	• the grave, particularly the pelvic area and the right hand were disturbed
KD271 [94]	• within the cemetery boundaries (Fig. 2a)	• rectangular with rounded corners, vertical walls, and an even bottom; •coffin (Supplementary Fig. 3a and b)	• length: 2.19 m; • width: 0.79 m; • depth: 0.63 m	•north-west to south-east (340°–160°) (Supplementary Fig. 3a and b)	• extended supine; •head to the north-west (tilted to the left); • feet to the south-east; • left arm placed at the side; •legs alongside each other (knees touching) (Supplementary Fig. 3a and b)	• iron buckle; • stone; •domestic sheep and chicken bones (Supplementary figure 3b)	• remains of ceramic vessels in the filling of the grave; • the grave, particularly the right side of the upper body and both feet were disturbed
KD518 [94]	• within the cemetery boundaries (Fig. 2a)	• rectangular with rounded corners, vertical walls, and an even bottom; •coffin (Supplementary Fig. 4a and b)	• length: 2.58 m; • width: 0.89 m; • depth: 0.41 m	•east to west (80°–260°) (Supplementary Fig. 4a and b)	• extended supine; •head to the east (tilted to the left); •feet to the west (tilted to the left); • arms placed at the sides; •legs alongside each other (knees touching) (Supplementary Fig. 4a and b)	• iron buckles; •iron knife (Supplementary figure 4b)	Ø
KD520 [95]	• within the cemetery boundaries (Fig. 2a)	• rectangular with rounded corners, vertical walls, and an even bottom; • coffin; • bed burial? (Supplementary Fig. 5a and b)	• length: 2.06 m; • width: 0.64 m; • depth: 0.57 m	•north-west to south-east (340°–160°) (Supplementary Fig. 5a and b)	• extended supine; •head to the north-west (tilted to the right); • feet to the south-east; • arms placed at the sides; •legs alongside each other (Supplementary Fig. 5a and b)	• spindle-whorl; •domestic chicken bones (Supplementary figure 5b)	•remains of a ceramic vessel in the filling of the grave; • the grave, particularly the right hand and both feet were disturbed
KK61 [95]	• within the cemetery boundaries (Fig. 2b)	• rectangular with rounded corners, vertical walls, and an even bottom; • ledges;	• length: 2.60 m; • width: 1.11 m; • depth: 0.71 m	• north-west to south-east (320°–140°) (Supplementary Fig. 6a and b)	• extended supine; • head to the north-west (tilted to the right); • feet to the south-east;	• iron knife; • iron buckles; • iron lamina; •domestic pig and chicken bones	Ø

(*continued on next page*)

Table 1 (*continued*)

Case IDs & References	BURIAL FEATURES						
	Location of the grave	Grave construction	Dimensions of the grave	Orientation of the grave	Positioning of the corpse	Grave goods	Other
		• bed burial? (Supplementary Fig. 6a and b)			• arms placed at the sides; •legs alongside each other (knees touching) (Supplementary Fig. 6a and b)	(Supplementary figure 6b)	
HC81 [93]	• within the cemetery boundaries (Fig. 2c)	• rectangular (Supplementary figure 7a)	• length: 1.81 m; • width: 0.48 m; • depth: 0.64 m	• north-west to south-east (321°–141°)	• extended supine; •head to the north-west (tilted to the right); • feet to the south-east; • left arm placed at the side; •legs alongside each other (Supplementary Fig. 7a and b)	•domestic sheep bones (Supplementary figure 7b)	• the grave, particularly the right upper extremity was disturbed
SS214 (presented in the current paper)	• within the cemetery boundaries (Fig. 2d)	• rectangular; • coffin (Supplementary figure 8a)	• length: 2.35 m; • width: 0.62–0.65 m; • depth: 0.50 m	•north-west to south-east (337°–157°) (Supplementary figure 8b)	• extended supine; • head to the north-west; • feet to the south-east; • arms placed at the sides; •legs alongside each other (Supplementary Fig. 8a and b)	• iron knife; • iron buckles; • iron objects; •bone tool (Supplementary figure 8b)	Ø

The Hajós–Cifrahegy and Sükösd–Ságod sites are located on the other side of the Danube-Tisza Interfluve, a few kilometres to the east from the Danube (Fig. 1); they are in close proximity to each other (~15 km). At Hajós–Cifrahegy (Fig. 2c and Supplementary text 3), the excavated 169 burials – originally the cemetery might have consisted of about 220–240 graves – are dated between from the middle of the 7th century CE to the beginning of the 9th century CE [98–103]. With 363 unearthed burials, Sükösd–Ságod (Fig. 2d and Supplementary text 4) is the largest of the four sites, which was established at the end of the 6th century CE and remained in use until the end of the 7th century CE/beginning of the 8th century CE [104–110].

With maybe the exception of Sükösd–Ságod, none of the aforementioned sites belong to the earliest phase of the Avar occupation in the Carpathian Basin or the Danube-Tisza Interfluve but were formed after the formation and establishment of the Avar Khaganate, during the Middle Avar period. Despite their differences in size and chronology, all of the four sites represent rural communities that presumably led a sedentary lifestyle.

2.2. Methods

To establish the definitive diagnosis of leprosy and to reconstruct the type and biological consequences of the disease in the eight individuals included in the current paper (**KD41**, **KD119**, **KD271**, **KD518**, **KD520**, **KK61**, **HC81**, and **SS214**), a detailed palaeopathological evaluation was performed on their skeletal remains. Before this analysis, their age-at-death was estimated [111–124] and sex was determined [125–127] using standard macromorphological methods of bioarchaeology. The results of these investigations can be found in Table 2. Information regarding the completeness and preservation of the eight examined skeletons were also recorded (Table 2 and Supplementary figures 1–8). During the palaeopathological evaluation, all skeletal remains of **KD41**, **KD119**, **KD271**, **KD518**, **KD520**, **KK61**, **HC81**, and **SS214** were macroscopically examined with the naked eye. This investigation focused on the detection of skeletal lesions that have been associated with HD in the palaeopathological literature:

1) Bony changes in the rhinomaxillary region of the face were registered considering the descriptions of Møller-Christensen and his colleagues [128], Møller-Christensen [129], and Andersen & Manchester [130]:
   - Surface pitting, progressive resorption, and eventual disappearance of the anterior nasal spine, with subsequent cortical capping at its original base;
   - Progressive, bilaterally symmetrical resorption and rounding/remodelling of the inferior and lateral margins of the pyriform aperture, with inferior widening of the anterior bony opening of the nasal cavity;
   - Progressive resorption, recession, and remodelling of the maxillary alveolar process (restricted largely to the premaxilla), with loosening and ultimate *ante-mortem* loss of the maxillary incisors;
   - Surface pitting, erosion, and thinning of the nasal and/or oral surfaces of the maxillary palatine process (sometimes accompanied by subperiosteal new bone formation), with eventual perforation of the hard palate; and
   - Surface pitting, progressive resorption, and ultimate disappearance of the intranasal bony structures, especially the bony nasal septum and the inferior nasal conchae;
2) Lesions of the small bones of the hands and feet were identified following the recommendations of Andersen & Manchester [131, 132], and Andersen and his co-workers [133,134]:
   - Palmar grooving at the distal end of the proximal hand phalanges;
   - Palmar bevelling at the proximal end of the middle hand phalanges;
   - Exostoses on the dorsal surface of the tarsal bones (at the attachment sites of the dorsal tarsal ligaments);
   - Concentric diaphyseal atrophy of the metacarpals, metatarsals, and hand and/or foot phalanges, with or without accompanying achro-osteolysis;

Table 2
Age-at-death, sex, completeness, and preservation of the eight examined skeletons – **KD41**, **KD119**, **KD271**, **KD518**, **KD520**, **KK61**, **HC81**, and **SS214**.

Case IDs, Age-at-death, & Sex (with references of the used methods)	PREDILECTION SITES OF LEPROSY								
	RHINOMAXILLARY REGION					POSTCRANIAL SKELETON			OTHER
	Anterior nasal spine	Pyriform aperture	Maxillary alveolar process	Maxillary palatine process	Intranasal bony structures	Hand bones	Lower leg bones	Foot bones	
KD41 **Middle-aged adult (40–59 years) [** [111, 113,115, 117–122,124]**]** **Male** [125–127]	• partially observable; • severely damaged *post-mortem*	• observable; • not damaged *post-mortem*	• observable; • not damaged *post-mortem*	• observable; • slightly damaged *post-mortem* (posteriorly)	• the left inferior nasal concha is observable and not damaged *post-mortem*; • the right inferior nasal concha is partially observable and damaged *post-mortem*; • the bony nasal septum is missing *post-mortem*	•only the scaphoid bone, the triquetrum, the hamate bone, the capitate bone, the trapezium, the five metacarpals, four (1st, 2nd, 3rd, and 4th) proximal phalanges, and the 1st distal phalanx are observable on the right side – they are slightly damaged *post-mortem*; •only the scaphoid bone, the lunate, the trapezium, the trapezoid bone, the capitate bone, the hamate bone, the five metacarpals, three (1st, 4th, and 5th) proximal phalanges, two (3rd and 4th) middle phalanges, and the 1st distal phalanx are observable on the left side – they are slightly damaged *post-mortem*	• observable; • the fibulae are moderately damaged *post-mortem*	• only the calcaneus, the talus, the navicular bone, the cuboid bone, the medial cuneiform bone, the five metatarsals, and three (3rd, 4th, and 5th) proximal phalanges are observable on the right side – the calcaneus, the 5th metatarsal, and the 5th proximal phalanx are severely, the other extant bones are slightly damaged *post-mortem*; • only the calcaneus, the talus, the navicular bone, the cuboid bone, two (medial and lateral) cuneiform bones, four (1st, 2nd, 3rd, and 5th) metatarsals, and four (1st, 2nd, 4th, and 5th) proximal phalanges are observable on the left side – the calcaneus and the 1st proximal phalanx are severely, the other extant bones are moderately damaged *post-mortem*	•the right maxillary sinus is not observable; • the orbital roofs are observable and not damaged *post-mortem*; • the femora are observable and slightly damaged *post-mortem*
KD119 **Middle-aged adult (40–59 years)** [111, 113,115, 117–119, 121–123] **Male** [125–127]	• partially observable; • severely damaged *post-mortem*	• observable; • not damaged *post-mortem*	• observable; • not damaged *post-mortem*	• partially observable; • severely damaged *post-mortem* (posteriorly)	• the right inferior nasal concha is observable and not damaged *post-mortem*; • the left inferior nasal concha and the bony nasal septum are missing *post-mortem*	•only the capitate bone, the triquetrum, the trapezium, the five metacarpals, four (2nd, 3rd, 4th, and 5th) proximal phalanges, and four (2nd, 3rd, 4th, and 5th) middle phalanges are observable on the right side – they are slightly damaged *post-mortem*; • only three (2nd, 3rd, and 4th) metacarpals, two (2nd and 4th) proximal phalanges, and the 2nd middle phalanx are observable on the left side – they are slightly damaged *post-mortem*	• the right tibia is missing *post-mortem*; •the left tibia and both fibulae are moderately damaged *post-mortem*	• only the calcaneus, the talus, two (medial and lateral) cuneiform bones, five metatarsals, and the 1st proximal phalanx are observable on the right side – the calcaneus, and the 4th and 5th metatarsals are severely, whereas the other extant bones are moderately damaged *post-mortem*; • only the calcaneus, the talus, the cuboid bone, the five metatarsals, and the 1st proximal phalanx are observable on the left side – the calcaneus, and the 4th and 5th metatarsals are severely, whereas the other extant bones are moderately damaged *post-mortem*	• the maxillary sinuses are not observable; •the orbital roofs are observable, but the right is moderately damaged *post-mortem*; • the femora are observable, but the right is slightly damaged *post-mortem*

(*continued on next page*)

Table 2 (*continued*)

Case IDs, Age-at-death, & Sex (with references of the used methods)	PREDILECTION SITES OF LEPROSY								
	RHINOMAXILLARY REGION					POSTCRANIAL SKELETON			OTHER
	Anterior nasal spine	Pyriform aperture	Maxillary alveolar process	Maxillary palatine process	Intranasal bony structures	Hand bones	Lower leg bones	Foot bones	
KD271 Middle-aged adult (40–59 years) [111, 113,115, 117–119, 121–123] **Male** [125–127]	• observable; • slightly damaged *post-mortem*	• observable; • not damaged *post-mortem*	• observable; • not damaged *post-mortem*	• partially observable; • severely damaged *post-mortem* (posteriorly)	•the inferior nasal conchae are observable and not damaged *post-mortem*; • the bony nasal septum is missing *post-mortem*	•only the 5th metacarpal, two (4th and 5th) proximal phalanges, the 4th middle phalanx, and the 1st distal phalanx are observable on the right side – they are not damaged *post-mortem*; •only the capitate bone, two (2nd and 3rd) metacarpals, three (1st, 3rd, and 5th) proximal phalanges, and the 3rd middle phalanx are observable on the left side – they are not damaged *post-mortem*	• observable; • not damaged *post-mortem*	• only the calcaneus, the talus, the navicular bone, two (2nd and 3rd) metatarsals, and two (2nd and 3rd) proximal phalanges are observable on the right side – they are slightly damaged *post-mortem*; • only the calcaneus, the talus, the navicular bone, the cuboid bone, two (2nd and 3rd) metatarsals, and the 2nd proximal phalanx are observable on the left side – they are slightly damaged *post-mortem*	•the left maxillary sinus is not observable; •the orbital roofs are observable, but the right is moderately damaged *post-mortem*; • the femora are observable and not damaged *post-mortem*
KD518 Younger to middle-aged adult (30–49 years) [[111, 113,115, 117–124]**] Male** [125–127]	• observable; • slightly damaged *post-mortem*	• observable; • not damaged *post-mortem*	• observable; • not damaged *post-mortem*	• observable; • not damaged *post-mortem*	• the inferior nasal conchae and the bony nasal septum are not observable, because they are severely damaged *post-mortem*	•only the scaphoid bone, the lunate, the pisiform bone, the hamate bone, the triquetrum, the trapezium, four (2nd, 3rd, 4th, and 5th) metacarpals, the five proximal phalanges, two (3rd and 4th) middle phalanges, and two (1st and 4th) distal phalanges are observable on the right side – the pisiform bone, and the 2nd and 5th metacarpals are moderately damaged *post-mortem*; • only the scaphoid bone, the capitate bone, the five metacarpals, three (3rd, 4th, and 5th) proximal phalanges, the 3rd middle phalanx, and the 3rd distal phalanx are observable on the left side – they are not damaged *post-mortem*	• the left tibia is missing *post-mortem*; •the right tibia and both fibulae are not damaged *post-mortem*	• only the calcaneus, the talus, the navicular bone, the cuboid bone, two (medial and intermediate) cuneiform bones, the five metatarsals, and two (2nd and 3rd) proximal phalanges are observable on the right side – the extant tarsal bones and the 5th metatarsal are slightly damaged *post-mortem*; • only the tarsal bones, the five metatarsals, the 1st proximal phalanx, and the 1st distal phalanx are observable on the left side – the calcaneus is slightly damaged *post-mortem*	• the maxillary sinuses are observable; • the left orbital roof is not observable, because it is severely damaged *post-mortem*; • the femora are observable, but the left is slightly damaged *post-mortem*
KD520 Younger adult (20–39 years) [[112,113, 116–124]**] Female** [125–127]	• observable; • not damaged *post-mortem*	• observable; • slightly damaged *post-mortem*	• observable; • not damaged *post-mortem*	• partially observable; • severely damaged *post-mortem*	• the inferior nasal conchae and the bony nasal septum are not observable, because they are severely damaged *post-mortem*	• only three (1st, 2nd, and 5th) metacarpals, and the 2nd proximal phalanx are observable on the right side – they are slightly damaged *post-mortem*; •only the capitate bone, the five metacarpals, three (2nd, 3rd, and 4th) proximal phalanges, three (2nd, 3rd, and 4th) middle phalanges, and the	• observable; • moderately damaged *post-mortem*	• only the tarsal bones, the five metatarsals, and the 5th proximal phalanx are observable on the right side – the calcaneus and the medial cuneiform bone are severely, whereas the other extant bones are moderately damaged *post-mortem*; • only two (1st and 2nd) metatarsals are observable on	• the maxillary sinuses are observable; • the orbital roofs are observable, but the right is severely damaged *post-mortem*; • the femora are observable, but

(*continued on next page*)

Table 2 (*continued*)

Case IDs, Age-at-death, & Sex (with references of the used methods)	PREDILECTION SITES OF LEPROSY								
	RHINOMAXILLARY REGION					POSTCRANIAL SKELETON			OTHER
	Anterior nasal spine	Pyriform aperture	Maxillary alveolar process	Maxillary palatine process	Intranasal bony structures	Hand bones	Lower leg bones	Foot bones	
						2nd distal phalanx are observable on the left side – they are not damaged *post-mortem*		the left side – they are moderately damaged *post-mortem*	slightly damaged *post-mortem*
KK61 **Middle-aged adult (40–59 years)** [111, 113,115, 117–119, 121–123] **Male** [125–127]	• observable; • not damaged *post-mortem*	• observable; • not damaged *post-mortem*	• observable; • not damaged *post-mortem*	• partially observable; • moderately damaged *post-mortem* (posteriorly)	• the inferior nasal conchae are observable and not damaged *post-mortem*; • the bony nasal septum is observable, but slightly damaged *post-mortem*	• only the scaphoid bone, four (1st, 2nd, 3rd, and 5th) metacarpals, four (1st, 2nd, 3rd, and 4th) proximal phalanges, and three (2nd, 3rd, and 4th) middle phalanges are observable on the right side – the scaphoid bone is severely, whereas the metacarpals are slightly damaged *post-mortem*; • only the five metacarpals, four (1st, 2nd, 3rd, and 4th) proximal phalanges, and the 3rd middle phalanx are observable on the left side – the 5th metacarpal is severely, the other extant bones are slightly damaged *post-mortem*	• observable; • the fibulae are severely, the tibiae are moderately damaged *post-mortem*	• only the calcaneus, the talus, the navicular bone, the cuboid bone, the medial cuneiform bone, and four (1st, 2nd, 3rd, and 4th) metatarsals are observable on the right side – the tarsal bones are severely, whereas the metatarsals are moderately damaged *post-mortem*; • only the calcaneus, the talus, the navicular bone, the cuboid bone, the medial cuneiform bone, and four (1st, 3rd, 4th, and 5th) metatarsals are observable on the left side – they are moderately damaged *post-mortem*	• the maxillary sinuses are not observable; • the orbital roofs are observable and not damaged *post-mortem*; • the femora are observable, but moderately damaged *post-mortem*
HC81 **Juvenile (16–18 years)** [114] **Female** [125]	• partially observable; • moderately damaged *post-mortem*	• observable; • not damaged *post-mortem*	• observable; • not damaged *post-mortem*	• observable; • not damaged *post-mortem*	• the left inferior nasal concha is missing *post-mortem*; • the bony nasal septum is partially observable, because it is severely damaged *post-mortem*	•no bones are observable on the right side; • only two (1st and 2nd) metacarpals, the 2nd proximal phalanx, and the 2nd middle phalanx are observable on the left side – the 2nd metacarpal is moderately damaged *post-mortem*	• observable; • moderately damaged *post-mortem*	• only the calcaneus, the talus, the cuboid bone, the medial cuneiform bone, and four (2nd, 3rd, 4th, and 5th) metatarsals are observable on the right side – they are severely damaged *post-mortem*; • no bones are observable on the left side	• the maxillary sinuses are not observable; • the orbital roofs are observable and not damaged *post-mortem*; • the femora are observable, but moderately damaged *post-mortem*
SS214 **Younger to middle-aged adult (30–49 years) [** [111, 113,117–119, 121,122]] **Male** [125–127]	• observable; • slightly damaged *post-mortem*	• observable; • not damaged *post-mortem*	• observable; • slightly damaged *post-mortem*	• partially observable; • moderately damaged *post-mortem* (posteriorly)	• the inferior nasal conchae are observable and slightly damaged *post-mortem*; • the bony nasal septum is not observable, because it is severely damaged *post-mortem*	•only the capitate bone, three (2nd, 4th, and 5th) metacarpals, and two (2nd and 5th) proximal phalanges are observable on the right side – they are slightly damaged *post-mortem*; • only three (1st, 2nd, and 3rd) metacarpals are observable on the left side – they are slightly damaged *post-mortem*	• the left tibia and fibula are missing *post-mortem*; •the right tibia and fibula are observable, but moderately damaged *post-mortem*	•only the talus, the navicular bone, the cuboid bone, the medial cuneiform bone, four (1st, 3rd, 4th, and 5th) metatarsals, and the 1st proximal phalanx are observable on the right side – the tarsal bones are moderately, whereas the metatarsals are slightly damaged *post-mortem*; •only the calcaneus, and three (3rd, 4th, and 5th) metatarsals are observable on the left side –	• the maxillary sinuses are partially observable; • the orbital roofs are observable, but they are moderately damaged *post-mortem*; • the left femur is missing *post-mortem;*

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Table 2 (*continued*)

Case IDs, Age-at-death, & Sex (with references of the used methods)	PREDILECTION SITES OF LEPROSY								
	RHINOMAXILLARY REGION					POSTCRANIAL SKELETON			OTHER
	Anterior nasal spine	Pyriform aperture	Maxillary alveolar process	Maxillary palatine process	Intranasal bony structures	Hand bones	Lower leg bones	Foot bones	
								the calcaneus is moderately, the metatarsals are slightly damaged *post-mortem*	• the right femur is observable, but moderately damaged *post-mortem*

- Septic bony changes of the small bones of the hands and/or feet (e.g., surface pitting, subperiosteal new bone formations, cortical erosion, and lytic or cystic lesions); and
- Septic articular changes of the joints of the hands and/or feet (e.g., subluxation, dislocation, and bony ankylosis);

3) Alterations of the long tubular bones of the lower legs were recorded following the guidelines of Andersen and his colleagues [134], Lewis and her co-workers [135], Schultz & Roberts [71], and Boel & Ortner [136]:
   - Surface pitting and/or subperiosteal new bone formations on the shaft of the lower leg bones, especially the distal half or two-thirds; and
   - Exostoses on the shaft of the lower leg bones (at the attachment sites of the crural interosseous membrane).

In addition to the above-mentioned palaeopathological diagnostic criteria for HD, signs of *cribra orbitalia* [137], maxillary sinusitis [138,139], and certain types of tooth pathologies (e.g., alveolar bone recession, and dental caries and calculus) [140,141] were also considered during the palaeopathological evaluation of the skeletal remains of **KD41**, **KD119**, **KD271**, **KD518**, **KD520**, **KK61**, **HC81**, and **SS214**, as these lesions have been frequently detected in cases with leprosy.

After the establishment of the diagnosis of leprosy, following the guidelines of Appleby and her colleagues [142], a slightly modified version of the Istanbul Protocol of the United Nations [143] was used to classify the eight examined individuals based on the degree of certainty of the diagnosis (Table 3). The following categories were distinguished: 1) not consistent with leprosy, 2) consistent with leprosy, 3) highly consistent with leprosy, 4) typical of leprosy, and 5) diagnostic of leprosy.

To investigate the mortuary treatment as related to leprosy and potential leprosy-related stigma and hereby, to reconstruct the social consequences of being affected by HD in the Avar-period Danube-Tisza Interfluve, features (location, construction, dimensions, and orientation of the grave, positioning of the corpse in the grave, and grave goods placed along with the deceased) of the burial of the eight individuals included in the current paper were also studied. The findings of this analysis can be found in Table 1. (It should be noted that unfortunately, because of the scanty documentation during excavation, only the supposed location of the burial of **HC81** can be marked in Fig. 2c.)

3. Results

In the eight examined individuals (**KD41**, **KD119**, **KD271**, **KD518**, **KD520**, **KK61**, **HC81**, and **SS214**), different areas of the skeleton displayed leprosy-related bony changes, including the rhinomaxillary region of the face, the small bones of the hands and feet, and the long tubular bones of the lower legs (Table 3). The most common location of skeletal lesions was the rhinomaxillary region with seven cases (**KD41**, **KD119**, **KD271**, **KD518**, **KK61**, **HC81**, and **SS214**), followed by the foot and lower leg bones with six cases (**KD41**, **KD271**, **KD520**, **KK61**, **HC81**, and **SS214**), and the hand bones with three cases (**KD41**, **KD271**, and **SS214**) (Table 3). There were only two individuals with solely rhinomaxillary alterations (**KD119** and **KD518**) and another one (**KD520**) with postcranial bony changes alone (in two locations: foot and lower leg bones) (Table 3). In the remaining five cases (**KD41**, **KD271**, **KK61**, **HC81**, and **SS214**), rhinomaxillary and postcranial lesions were concomitantly present; in the postcranial skeleton of three out of these five individuals (**KD41**, **KD271**, and **SS214**), not only the foot and lower leg bones but also the hand bones provided evidence of HD (Table 3). In the current paper, only the newly discovered probable case with HD from the Sükösd–Ságod site (**SS214**) is demonstrated in detail (Figs. 3–11 and Table 3). For comparison purposes, the macroscopic leprosy-related skeletal lesions that were recorded during the re-evaluation of the seven already published cases with HD from the Avar-period Danube-Tisza Interfluve (**KD41**, **KD119**, **KD271**, **KD518**,

Table 3
Registered bony changes indicative of leprosy in the eight examined skeletons – **KD41**, **KD119**, **KD271**, **KD518**, **KD520**, **KK61**, **HC81**, and **SS214**.

Case IDs & References	REGISTERED BONY CHANGES INDICATIVE OF LEPROSY								
Degree of certainty of the diagnosis	RHINOMAXILLARY REGION					POSTCRANIAL SKELETON			OTHER
	Anterior nasal spine	Pyriform aperture	Maxillary alveolar process	Maxillary palatine process	Intranasal bony structures	Hand bones	Lower leg bones	Foot bones	
KD41 [86] **"typical of leprosy"**	•partial resorption; • slight surface pitting around the base	• slight inferior widening; • slight, bilaterally symmetrical resorption and rounding/ remodelling of the lateral and inferior margins; • vascular impressions on the inferior margins	Ø	• slight pitting on the oral surface	• complete resorption of the left inferior nasal concha	• marginal palmar osteophytes on the shaft of the middle and proximal phalanges	• surface pitting and longitudinally striated subperiosteal new bone formations on the shaft of both tibiae and fibulae; • exostoses on the shaft of both tibiae and fibulae (at the attachment sites of the crural interosseous membrane)	• septic bony changes (e.g., pitting and/or subperiosteal new bone formations) on the plantar and dorsal surfaces of the metatarsals; • exostoses on the dorsal surface of the tarsal bones (at the attachment sites of the dorsal tarsal ligaments)	• alveolar bone recession in the maxillae and mandible; • dental calculus and/or caries on the maxillary and mandibular teeth with secondary *ante-mortem* tooth loss; • pitting and slight subperiosteal new bone formations in the left maxillary sinus; • exostoses on the *linea aspera* of both femora
KD119 [86] **"highly consistent with leprosy"**	• slight surface pitting around the base	• very slight inferior widening; •very slight, bilaterally symmetrical resorption and rounding/ remodelling of the inferior margins	Ø	• slight pitting on the oral surface	• surface pitting and partial resorption of the right inferior nasal concha	Ø	Ø	Ø	• alveolar bone recession in the maxillae and mandible; • dental calculus on the maxillary and mandibular teeth; • slight surface pitting at the lateral margins of the pyriform aperture (upper part); • slight surface pitting and partial resorption of the nasal bones at the internasal suture
KD271 [86,88] **"diagnostic of leprosy"**	•complete resorption; • cortical capping at the original base	• inferior widening; •bilaterally symmetrical resorption and rounding/remodelling of the lateral and inferior margins; •vascular impressions on the inferior margins	•slight resorption at the prosthion; • damage to the alveoli of the maxillary central incisors	• extensive pitting and erosion on the nasal surface; • slight pitting on the oral surface; • irregular, sharp-edged perforation on the left side	• complete resorption of the inferior nasal conchae; • partial (inferior) absorption of the bony nasal septum	• palmar grooving at the distal end of the proximal phalanges; •palmar bevelling at the proximal end of the middle phalanges; • marginal palmar osteophytes on	• surface pitting and longitudinally striated subperiosteal new bone formations on the shaft of both tibiae and fibulae (distal part); • exostoses on the shaft of both tibiae and fibulae (at the attachment sites of	• exostoses on the dorsal surface of the tarsal bones (at the attachment sites of the dorsal tarsal ligaments)	•alveolar bone recession in the maxillae; • *ante-mortem* loss of the left maxillary central incisor; • dental caries on the maxillary teeth; • subperiosteal new bone formations in

(*continued on next page*)

Table 3 (*continued*)

Case IDs & References	REGISTERED BONY CHANGES INDICATIVE OF LEPROSY								
Degree of certainty of the diagnosis	RHINOMAXILLARY REGION					POSTCRANIAL SKELETON			OTHER
	Anterior nasal spine	Pyriform aperture	Maxillary alveolar process	Maxillary palatine process	Intranasal bony structures	Hand bones	Lower leg bones	Foot bones	
						the shaft of the middle and proximal phalanges	the crural interosseous membrane)		the right maxillary sinus; • exostoses on the *linea aspera* of both femora
KD518 [86] **"consistent with leprosy"**	•slight surface pitting around the base	•vascular impressions on the left inferior margin	• very slight resorption at the prosthion	Ø	Ø	Ø	Ø	Ø	• alveolar bone recession in the maxillae; • dental calculus on the maxillary teeth
KD520 [86,88] "**consistent with leprosy**"	Ø	Ø	Ø	Ø	Ø	Ø	• surface pitting and longitudinally striated subperiosteal new bone formations on the shaft of both tibiae and fibulae	• concentric diaphyseal atrophy of a proximal phalanx (true pan-circumferential concentric type) and three metatarsals (knife-edge type); • septic bony changes (e.g., pitting and/or subperiosteal new bone formations) on the plantar and dorsal surfaces of the metatarsals, and the medial surface of the right calcaneus	• bilateral *cribra orbitalia*; • dental calculus on the maxillary and mandibular teeth
KK61 [86,89] "**diagnostic of leprosy**"	• complete resorption; •cortical capping at the original base	• inferior widening; • bilaterally symmetrical resorption and rounding/remodelling of the lateral and inferior margins	•slight resorption at the prosthion; • damage to the alveoli of the maxillary incisors	• pitting, erosion, and thinning on the oral and nasal surfaces; • irregular, sharp-edged perforation at the posterior half	• complete resorption of the inferior nasal conchae; • partial (inferior) absorption of the bony nasal septum	Ø	• surface pitting and longitudinally striated subperiosteal new bone formations on the shaft of both tibiae and fibulae; • exostoses on the shaft of both tibiae and fibulae (distally, at the attachment sites of the crural interosseous membrane)	• exostoses on the dorsal surface of the tarsal bones (at the attachment sites of the dorsal tarsal ligaments); • septic bony changes (e.g., pitting and/or subperiosteal new bone formations) on the plantar and dorsal surfaces of the metatarsals	• alveolar bone recession in the maxillae and mandible; • dental calculus and/or caries on the maxillary and mandibular teeth; • *ante-mortem* loss of the maxillary central incisors; • exostoses on the *linea aspera* of both femora
HC81 [87] "**diagnostic of leprosy**"	• surface pitting around the base	• inferior widening; • bilaterally symmetrical resorption and rounding/remodelling of the lateral and inferior margins;	• resorption at the prosthion; • damage to the alveoli of the maxillary central incisors	• slight pitting and erosion on the nasal surface; • extensive pitting, erosion, and thinning on the oral surface; • two irregular, sharp-edged	• slight surface pitting of the right inferior nasal concha; • partial absorption of the bony nasal septum (not only the vomer but also the perpendicular	Ø	• surface pitting and longitudinally striated subperiosteal new bone formations on the shaft of both tibiae	• septic bony changes (slight pitting) on the medial surface of the right calcaneus	• alveolar bone recession in the maxillae and mandible; • dental calculus on the maxillary and mandibular teeth; • pitting on the horizontal plate of

(*continued on next page*)

Table 3 (*continued*)

Case IDs & References	REGISTERED BONY CHANGES INDICATIVE OF LEPROSY								
Degree of certainty of the diagnosis	RHINOMAXILLARY REGION					POSTCRANIAL SKELETON			OTHER
	Anterior nasal spine	Pyriform aperture	Maxillary alveolar process	Maxillary palatine process	Intranasal bony structures	Hand bones	Lower leg bones	Foot bones	
		•vascular impressions on the left inferior margin		perforations on both maxillae (close to the midline)	lamina of the ethmoid bone)				both palatine bones; • surface pitting and subperiosteal new bone formations on the distal end of the left humerus (lateral side); • surface pitting on the proximal end of the left ulna (lateral side)
SS214 (presented in the current paper) "**typical of leprosy**"	• slight surface pitting around the base (Fig. 3)	• a small, well-circumscribed osteolytic lesion with irregular, thickened edges at the upper part of the right lateral margin surrounded by surface pitting (Fig. 4a); • vascular impressions on the inferior margins (Fig. 4b)	• very slight resorption at the prosthion (Fig. 5); • very slight damage to the alveoli of the maxillary central incisors (Fig. 5)	• very slight pitting and subperiosteal new bone formations on the oral surface (Fig. 6)	• almost complete resorption of the inferior nasal conchae (Fig. 7)	• palmar grooving at the distal end of the proximal phalanges (Fig. 9); • marginal palmar osteophytes on the shaft of the proximal phalanges (Fig. 9)	• surface pitting and longitudinally striated subperiosteal new bone formations on the shaft of the right tibia and fibula (Fig. 11)	• concentric diaphyseal atrophy (knife-edge type) of four metatarsals (Fig. 10)	• slight alveolar bone recession in the maxillae and mandible (Fig. 8b); • dental calculus on the maxillary teeth (Fig. 8a); • dental caries on the mandibular teeth with secondary abscess formation and *ante-mortem* tooth loss (Fig. 8c)

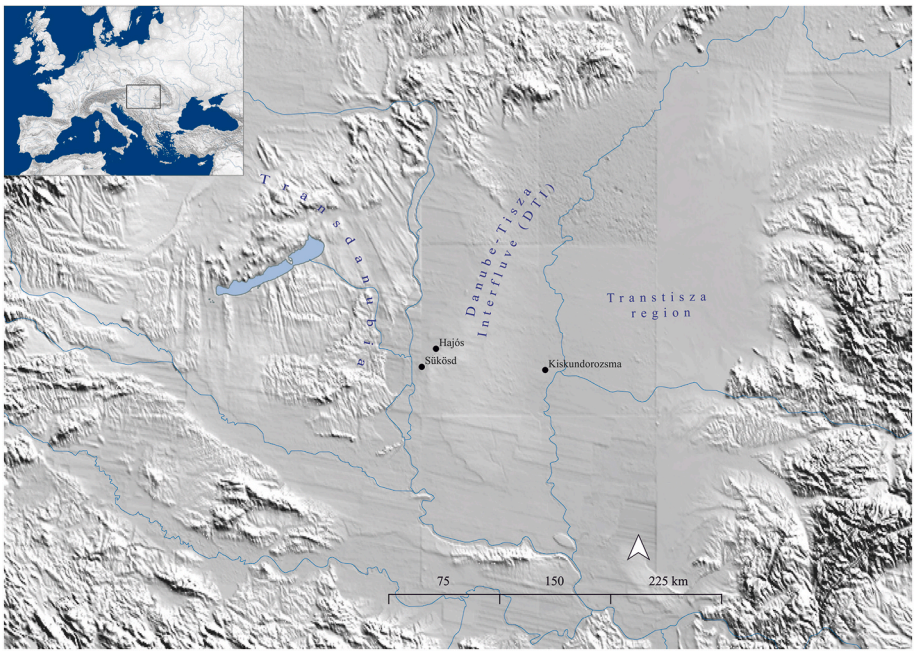

Fig. 1. Map showing the location of the Kiskundorozsma–Daruhalom-dűlő II, Kiskundorozsma–Kettőshatár I, Hajós–Cifrahegy, and Sükösd–Ságod archaeological sites in the Danube-Tisza Interfluve (source of map: Global Multi-resolution Terrain Elevation Data 2010 (GMTED2010) of the U.S. Geological Survey (USGS), and Natural Earth – free vector and raster map data @ naturalearthdata.com).

KD520, **KK61**, and **HC81**) are summarised in Table 3.

3.1. Cranial bony changes in SS214

In the rhinomaxillary region of the face, numerous skeletal lesions indicative of leprosy were registered (Figs. 3–8 and Table 3). Although the *post-mortem* damages precluded the definitive observation of the anterior nasal spine, slight surface pitting was detected around its base (Fig. 3). The upper part of the right lateral margin of the pyriform aperture presented a small (~2 mm in width and 3 mm in height), well-circumscribed osteolytic lesion with irregular, thickened edges; it was surrounded by very slight surface pitting (Fig. 4a). Furthermore, the inferior margins of the pyriform aperture exhibited abnormal vascular impressions (Fig. 4b). Although it was slightly damaged *post-mortem*, the maxillary alveolar process revealed very slight resorption at the prosthion; the alveoli of the central incisors were very slightly damaged (inferiorly) (Fig. 5). On the anterior part of the oral surface of the maxillary palatine process, slight abnormal pitting and very slight subperiosteal new bone formations were observed (Fig. 6). Due to *post-mortem* damages, the examination of the intranasal bony structures was hindered, but it seems that both inferior nasal conchae were almost completely resorbed (Fig. 7). At the cemento-enamel junction, all maxillary and mandibular teeth showed slight recession of the alveolar bone (Fig. 8b). There were signs of dental caries on the left lower first and third molars, with secondary abscess formation at the former one (Fig. 8c); it cannot be excluded that the *ante-mortem* loss of the left lower second molar and the right lower first molar was due to caries. Finally, dental calculus (right upper first and second premolars and molars) (Fig. 8a) and linear enamel hypoplasia (left and right upper and lower canines, and right lower lateral incisor) (Fig. 8d) were also recorded on some of the maxillary and/or mandibular teeth.

3.2. Postcranial bony changes in SS214

In the postcranial skeleton, two proximal phalanges of the right hand (Fig. 9), some metatarsals of the feet (Fig. 10), and the long tubular bones of the right lower leg (Fig. 11) displayed skeletal lesions that are indicative of leprosy (Table 3). In the juxta-articular area at the distal end of the right 2nd and 5th proximal phalanges, a shallow groove was present across the entire width of the palmar surface (Fig. 9). Moreover, on both sides of the diaphysis of these phalanges, marginal osteophytes were registered on the palmar surface (Fig. 9). The lateromedial diameter of the diaphysis of the left and right 3rd and 4th metatarsals was decreased, giving the affected bones a knife-shaped appearance where the superior border of the diaphysis became sharp (Fig. 10). The right tibia showed surface pitting and longitudinally striated subperiosteal new bone formations (with a more or less organised, lamellar-like macroscopic appearance) throughout the length of the shaft, especially on the medial surface (Fig. 11a). Although the substantial *post-mortem* damages precluded the definitive observation of the right fibula, some patches of surface pitting and longitudinally striated subperiosteal new bone formations (with a more or less organised, lamellar-like macroscopic appearance) were detected on the lateral and medial surfaces of its shaft (Fig. 11b).

4. Discussion

4.1. Biological aspects

In the current paper, eight cases with HD from the Avar-period Danube-Tisza Interfluve (**KD41**, **KD119**, **KD271**, **KD518**, **KD520**, **KK61**, **HC81**, and **SS214**) were subject to a detailed palaeopathological analysis that concentrated on the detection of leprosy-related skeletal lesions. Based on the macroscopic characteristics and distribution pattern of the recorded alterations, not only the retrospective diagnosis of HD was established but the type and biological consequences of the disease were also reconstructed in every case.

4.1.1. Demographic distribution

Almost all of the examined individuals (7 cases – **KD41**, **KD119**, **KD271**, **KD518**, **KD520**, **KK61**, and **SS214**) were of adult age – four middle-aged adults (**KD41**, **KD119**, **KD271**, and **KK61**; 40–59 years), two younger to middle-aged adults (**KD518** and **SS214**; 30–59 years), and one younger adult (**KD520**; 20–39 years) (Table 2). There was only one skeletally immature individual (**HC81**), who died as a late adolescent (16–18 years) (Table 2). The majority of the examined individuals

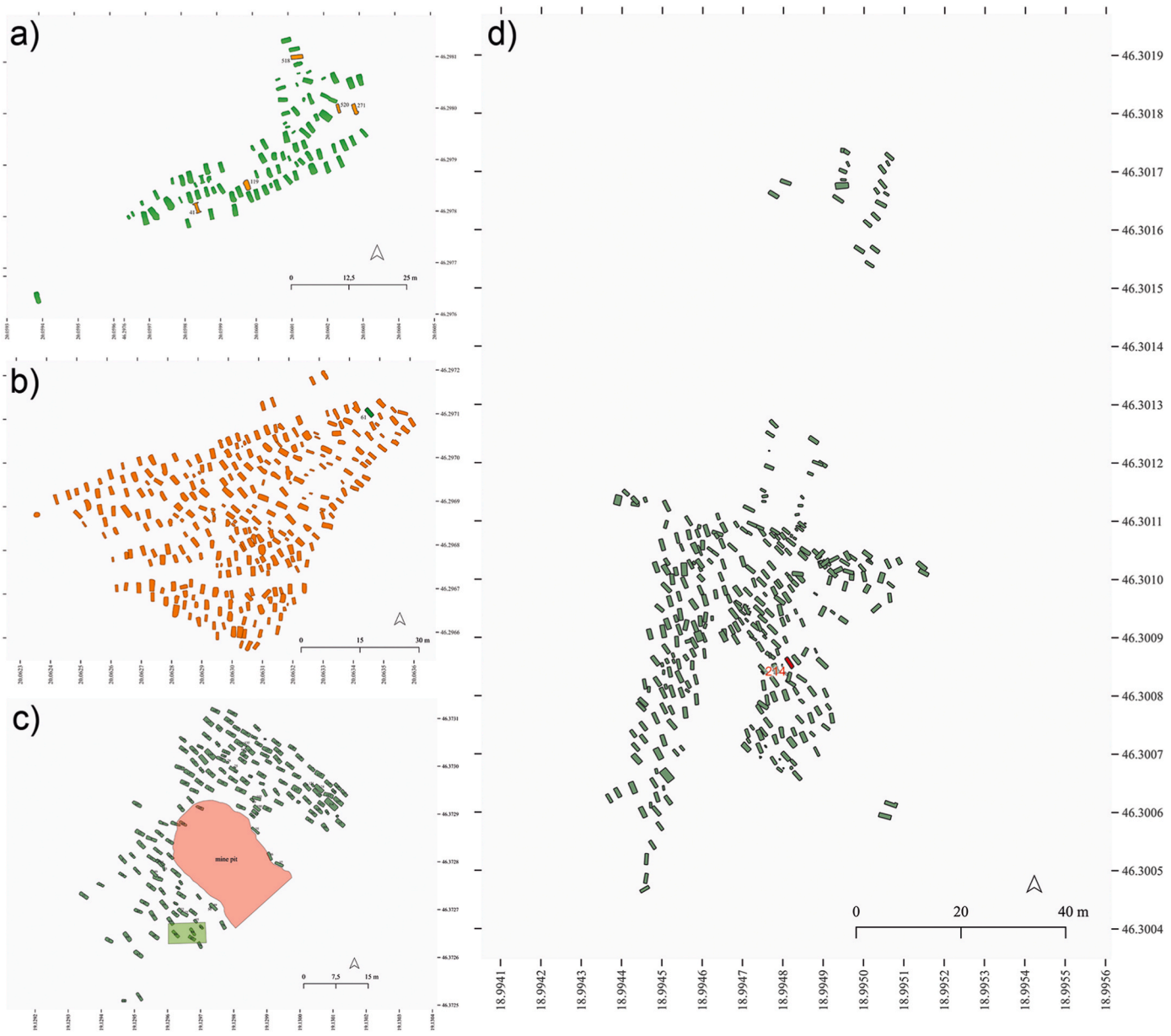

Fig. 2. a) Plan drawing of the Kiskundorozsma–Daruhalom-dűlő II cemetery with the location of the burials of **KD41**, **KD119**, **KD271**, **KD518**, and **KD520** (highlighted in orange); b) Plan drawing of the Kiskundorozsma–Kettőshatár I cemetery with the location of the burial of **KK61** (highlighted in green); c) Plan drawing of the Hajós–Cifrahegy cemetery with the supposed location of the burial of **HC81** (green rectangle); and d) Plan drawing of the Sükösd–Ságod cemetery with the location of the burial of **SS214** (highlighted in red) (source of maps a) and b): Archaeological Database of the Móra Ferenc Museum, Szeged, Hungary; and source of maps c) and d): Archaeological Database of the Türr István Museum, Baja, Hungary). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

were males (6 cases – **KD41**, **KD119**, **KD271**, **KD518**, **KK61**, and **SS214**); only the two youngest individuals (**KD520** and **HC81**) were determined as females by the secondary sexual characteristics of their skeletons (Table 2). These findings fit in with those of epidemiological studies, as leprosy appears to be much more prevalent in adults than in children under the age of 15 years; the long incubation period of the disease can be a factor behind this trend [144–147]. In addition, there seems to be a preponderance of male over female patients, with women affected by HD being generally younger than men [148–150]. It cannot be excluded that hormonal changes (e.g., during pregnancy and lactation) and the consequent alteration in the host's immune status may be responsible for women to be more frequently affected by leprosy in their reproductive age [149–152].

4.1.2. Disease type

Although bony changes can occur at and between both ends of the disease spectrum of leprosy, and it is assumed that their type, severity, and distribution pattern correspond to the host's immune status and consequently, to the form of HD the patient had, it can be challenging to distinguishing between the different types of the disease in past populations [69,70,73,135,153,154]. In near-TT or TT, which are characterised by a high resistance to leprosy bacilli, the skeleton may not be affected but if it is, alterations may occur solely in the postcranial elements, with involvement of the skeleton being either unilateral or bilateral; the expression of the lesions is usually asymmetrical [135,153,155]. On the other hand, in near-LL or LL, which are characterised by a low resistance to leprosy bacilli, there is always the presence of rhinomaxillary bony changes, usually with simultaneous involvement of the

Fig. 3. Slight surface pitting around the base of the anterior nasal spine of **SS214**.

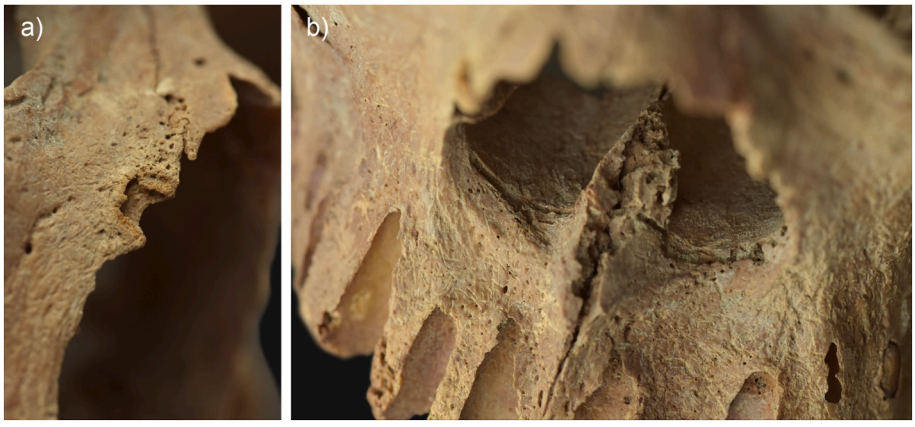

Fig. 4. a) A small (~2 mm in width and 3 mm in height), well-circumscribed osteolytic lesion with irregular, thickened edges on the upper part of the right lateral margin of the pyriform aperture of **SS214**; and b) Abnormal vascular impressions on the inferior margins of the pyriform aperture of **SS214**.

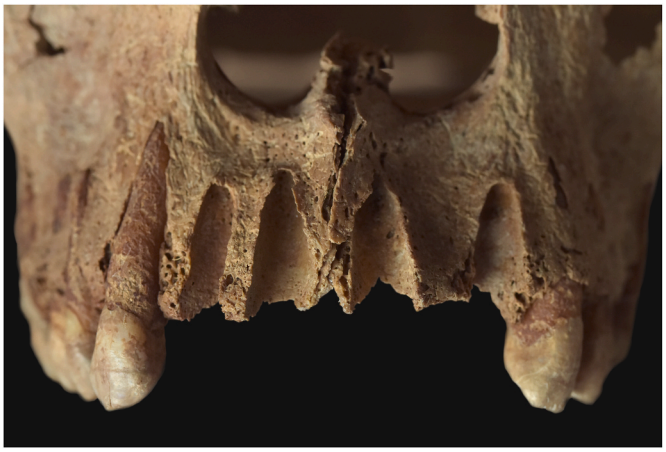

Fig. 5. Very slight resorption of the maxillary alveolar process of **SS214** at the prosthion, with very slight damage to the alveoli of the maxillary central incisors.

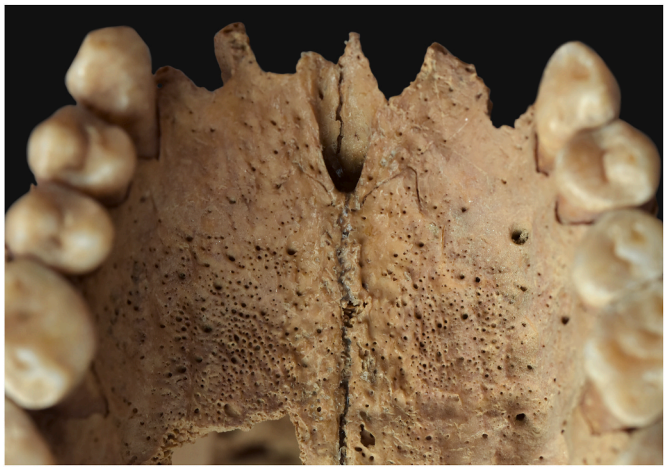

Fig. 6. Slight abnormal pitting and very slight subperiosteal new bone formations on the anterior part of the oral surface of the maxillary palatine process of **SS214**.

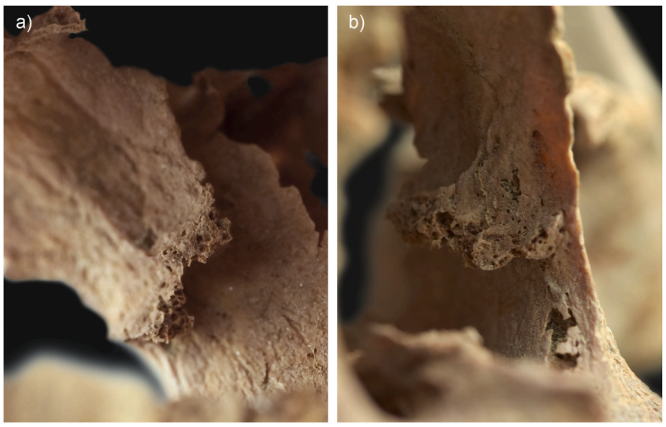

Fig. 7. Almost complete resorption of the inferior nasal conchae of **SS214**: a) right side and b) left side.

postcranial elements (in at least one location); the involvement of the skeleton is usually bilateral with a symmetrical lesion expression [135,153,155]. Based on the above, almost all of the examined individuals could have suffered from near-LL or LL (7 cases – **KD41**, **KD119**, **KD271**, **KD518**, **KK61**, **HC81**, and **SS214**) (Table 3). There was only one individual (**KD520**), who could have represented near-TT or TT (Table 3). These findings are not surprising if we consider that the majority of leprosy cases identified in past populations are of the LL type – the long well-known and widely used palaeopathological diagnostic criteria, the so-called rhinomaxillary syndrome (RMS) is pathognomonic for LL, which makes the establishment of a diagnosis easier [56,72,156]. On the other hand, the research for palaeopathological diagnostic criteria for TT does not go back a long time and the postcranial bony changes indicative of this disease form (or even their association) cannot be considered as specific for leprosy, making the recognition of TT very difficult [56,72,153,155].

4.1.3. Biological consequences

In the rhinomaxillary region of the face, direct invasion of the bones by leprosy bacilli, either through contiguous extension of the infection from the overlying soft tissues (e.g., skin and oronasal mucosa) or haematogenous dissemination of the pathogens, gives rise to the formation of a set of skeletal lesions (RMS), the distribution of which reflects the cooler temperature of exposed skin and oronasal mucosa; it is consistent with the well-known temperature preference of leprosy bacilli [69,70,72,130,154,157]. RMS is a composite mixture of absorptive, erosive, and proliferative alterations that involve 1) the anterior nasal spine, 2) the pyriform aperture (especially its inferior and lateral margins), 3) the maxillary alveolar process, 4) the maxillary palatine process, and 5) the intranasal bony structures (e.g., inferior nasal conchae and bony nasal septum) [70,71,130,157]. From the seven individuals with near-LL or LL (**KD41**, **KD119**, **KD271**, **KD518**, **KK61**, **HC81**, and **SS214**), six (**KD41**, **KD119**, **KD271**, **KK61**, **HC81**, and **SS214**) revealed at least four out of the five anatomical components of RMS, whereas one (**KD518**) displayed only two (Table 3). The most common location of bony changes was the anterior nasal spine with seven cases (**KD41**, **KD119**, **KD271**, **KD518**, **KK61**, **HC81**, and **SS214**), followed by the maxillary palatine process and the intranasal bony structures with six cases (**KD41**, **KD119**, **KD271**, **KK61**, **HC81**, and **SS214**), and the pyriform aperture (**KD41**, **KD119**, **KD271**, **KK61**, and **HC81**) and the maxillary alveolar process (**KD518**, **KD271**, **KK61**, **HC81**, and **SS214**) with five cases (Table 3). It should be noted that the *post-mortem* missing or damages precluded the definitive observation of at least some of the anatomical components of RMS in every individual included in the current paper (Table 2).

In all the seven individuals with RMS (**KD41**, **KD119**, **KD271**, **KD518**, **KK61**, **HC81**, and **SS214**), the initial site of the leprous infection could have been the nasal mucosa (i.e., the mucous membrane lining the nasal cavity). It could have been infiltrated by leprosy bacilli following inhalation of the pathogens, which could have resulted in the onset of atrophic rhinitis (i.e., progressive thinning and hardening of the nasal mucosa), a condition characterised by symptoms of highly bacilliferous, muco-purulent or exudative, foul-smelling nasal discharges, dry, thick nasal crusts, recurrent epistaxis, and obstruction of the nasal airways [69,130,158–161]. In two individuals (**KD41** and **KD271**), based on the presence of pitting and/or subperiosteal new bone formations on the walls of the left and right maxillary sinuses, respectively (Table 3), the leprous infection could have extended from the nasal cavity to the aforementioned paranasal sinuses; signs of maxillary sinusitis have been frequently recorded in cases with RMS [72,138,139,154,161]. As the

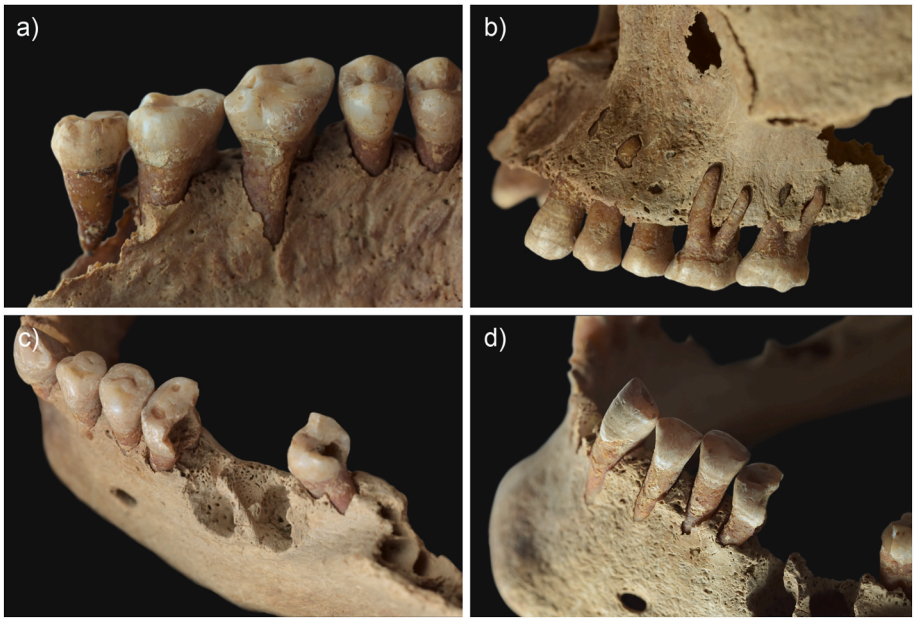

Fig. 8. a) Dental calculus on the right upper first and second premolars and molars of **SS214**; b) Slight recession of the maxillary alveolar bone of **SS214** (left side); c) Dental caries on the left lower first and third molars of **SS214**, with secondary abscess formation at the former one, and *ante-mortem* loss of the left lower second molar of **SS214**; and d) Linear enamel hypoplasia on the left lower canine of **SS214**.

Fig. 9. A shallow groove across the entire width of the palmar surface of the distal end of the right 2nd and 5th proximal phalanges of **SS214** in the juxta-articular area, with marginal osteophytes on both sides of the affected diaphyses.

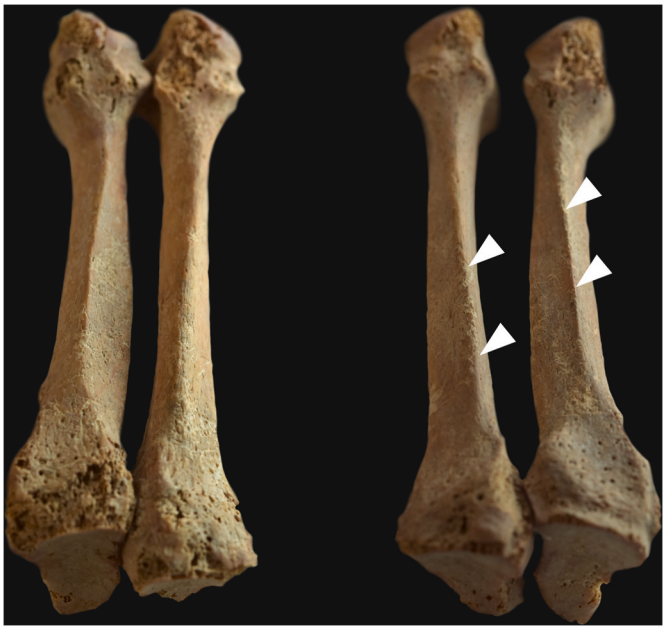

Fig. 10. Concentric (knife-edge type) diaphyseal atrophy of the left and right 3rd and 4th metatarsals of **SS214**, with the superior border of the diaphyses becoming sharp (white arrows).

pathological process progressed in the seven individuals with RMS (**KD41**, **KD119**, **KD271**, **KD518**, **KK61**, **HC81**, and **SS214**), not only the nasal mucosa but the underlying cartilaginous and bony nasal structures (e.g., anterior nasal spine, nasal surface of the maxillary palatine process, and nasal septum) could have become affected by HD, with subsequent development of the observed bony changes (e.g., partial or

Fig. 11. Surface pitting and longitudinally striated subperiosteal new bone formations on the shaft of the right a) tibia (medial surface) and b) fibula (lateral surface) of **SS214**.

complete resorption, and surface pitting, erosion, and thinning) (Table 3) [130,158,159]. In three cases (**KD271**, **KK61**, and **HC81**), where there was evidence of the partial (inferior) absorption of the bony nasal septum (Table 3), it can be presumed that loss of the cartilaginous and bony support in the nose could have led to the development of 'saddle-nose' deformity (i.e., abnormal concavity of the nasal dorsum) [7,69,130,159,162]. Saddle-nose deformity is characteristic of advanced-stage LL; it can be associated with aesthetic repercussions (e.g., facial disfigurement) and functional implications (e.g., impaired nasal breathing) [130,140,159,162]. In the aforementioned three individuals (**KD271**, **KK61**, and **HC81**), there could have been persistent blockage of the nasal airways, which could have made it difficult for them to breathe through their nose. As a consequence of this, they could have developed an oral breathing habit, which seems to be a common accompaniment of LL today [140,163,164]. It should be noted that in the four other cases with RMS (**KD41**, **KD119**, **KD518**, and **SS214**), where the bony nasal septum was not observable due to *post-mortem* missing or damages (Table 2), even the atrophic rhinitis alone, which develops early in the pathogenesis of leprosy, could have resulted in obstruction of the nasal airways, with subsequent impaired nasal breathing and long-standing breathing through the mouth. Furthermore, even if the presence of saddle-nose deformity cannot be evaluated in **KD41**, **KD119**, **KD518**, and **SS214**, the facial soft-tissue (e.g., skin and oronasal mucosa) lesions alone could have led to aesthetic repercussions in these cases.

Chronic oral breathing can have a negative impact on oral health (e.g., it can increase the risk of developing periodontitis, dental caries or calculus), as it can contribute to changes in the intraoral humidification, pH, and oxygen levels [165,166]. Based on the above, it cannot be excluded that HD and the resultant long-standing breathing through the mouth could have been at least partially responsible for the tooth pathologies (e.g., dental caries and calculus, *ante-mortem* tooth loss, and alveolar bone recession) that were recorded in the seven individuals with RMS (**KD41**, **KD119**, **KD271**, **KD518**, **KK61**, **HC81**, and **SS214**) (Table 3). In six out of these seven cases (**KD41**, **KD119**, **KD271**, **KD518**, **KK61**, and **HC81**), the severity of the detected alveolar bone loss in the mandible and/or maxillae implies that these individuals had advanced-stage periodontitis (i.e., severe inflammation of the gums); and thus, they would have suffered from pronounced halitosis (i.e., bad breath) [167,168]. During oral breathing, there is a decrease in the surface temperature of certain areas of the oral cavity (e.g., anterior part of the maxilla, and soft and hard palates) due to the cooling effect of the inspired air and evaporation [163,164,169,170]. The lower surface temperature makes the mucous membrane of these oral sites more prone to seeding by leprosy bacilli; and thus, to developing leprous lesions [163,164,170]. Later, usually as a result of contiguous spread of the

infection, not only the oral mucosa but the underlying bone (e.g., the premaxilla or the oral surface of the maxillary palatine process) can become affected by leprosy, with consequent formation of oral skeletal lesions [130,163,164]. All of the seven individuals with RMS (**KD41**, **KD119**, **KD271**, **KD518**, **KK61**, **HC81**, and **SS214**) displayed oral bony changes: five (**KD271**, **KD518**, **KK61**, **HC81**, and **SS214**) revealed resorption of the prosthion of varying severity, whereas six (**KD41**, **KD119**, **KD271**, **KK61**, **HC81**, and **SS214**) presented pitting, erosion, and/or thinning of the oral surface of the maxillary palatine process (Table 3). In three out of these cases (**KD271**, **KK61**, and **HC81**), leprous involvement of both the oral and nasal surfaces of the maxillary palatine process could have led to the ultimate perforation of the hard palate (Table 3). The development of the observed irregular, sharp-edged perforations could have been accompanied by the formation of an oro-nasal fistula (i.e., an abnormal communication between the oral and nasal cavities), the presence of which could have given rise to functional difficulties (e.g., speech impairments and nasal regurgitation of food or liquids) in **KD271**, **KK61**, and **HC81** [140,164,171]. It should be noted that oral skeletal lesions (e.g., perforation of the hard palate) are usually late phenomena of LL [130,163,164].

In the postcranial skeleton, it is the neuropathy in the sensory, motor, and/or autonomic peripheral nerves rather than the direct invasion of the bones by leprosy bacilli that is responsible for the development of skeletal lesions; these bony changes are not pathognomonic but highly characteristic of HD [69,134]. Infiltration of the peripheral nerve tissue by the pathogens and its subsequent inflammation leads to the loss of sensory, motor, and/or autonomic functions in the affected nerves; characteristically the large, superficial peripheral nerves (e.g., ulnar and posterior tibial) are involved in leprosy [34,69,131,132,172]. From the eight examined individuals (**KD41**, **KD119**, **KD271**, **KD518**, **KD520**, **KK61**, **HC81**, and **SS214**), six (**KD41**, **KD271**, **KD520**, **KK61**, **HC81**, and **SS214**) revealed postcranial alterations that are suggestive of leprous peripheral neuropathy (Table 3). The most common lesion locations were the foot and lower leg bones with six cases (**KD41**, **KD271**, **KD520**, **KK61**, **HC81**, and **SS214**), followed by the hand bones with three cases (**KD41**, **KD271**, and **SS214**) (Table 3). It should be noted that the *post-mortem* missing or damages precluded the definitive observation of at least some of the postcranial predilection sites of HD, especially the hand and foot bones, in every individual included in the current paper (Table 2).

In all of the six individuals with postcranial bony changes (**KD41**, **KD271**, **KD520**, **KK61**, **HC81**, and **SS214**), the hand and/or foot bones provided direct or indirect evidence for the loss of sensory function in the ulnar and/or posterior tibial nerves, respectively (Table 3). In four out of these six cases (**KD41**, **KD520**, **KK61**, and **HC81**), leprous dysfunction of the sensory component of the posterior tibial nerve, which supplies sensation to the plantar foot, could have resulted in diminution or complete loss of one or more sensation modalities (e.g., temperature, pain or touch); eventually all of them could have become affected by HD [131,134,172,173]. Usually, it is the most superficial, coolest distal terminal branches of the posterior tibial nerve, from where the pathological process commences [34,172,173]. Early in the course of the disease, due to leprous involvement of these dermal sensory nerve fibres, there could have been gradual and progressive loss of the cutaneous sensation in circumscribed areas, with consequent development of anaesthetic skin patches in the feet of **KD41**, **KD520**, **KK61**, and **HC81** [34,173]. The insensitive feet of these four individuals could have become more prone to unintentional, minor, superficial trauma of the affected skin area(s) (e.g., burns or cuts) [69,134,135,173]. The repeated, unperceived traumata to the soft tissues of the feet of **KD41**, **KD520**, **KK61**, and **HC81** could have given rise to aseptic inflammation, with the inflamed area(s) undergoing aseptic tissue necrosis secondary to local vascular damage and haemorrhage (i.e., chronic superficial insensitive ulceration) [134]. As the aseptic necrotic area(s) (i.e., the aseptic ulcer(s)) could have provided a portal of entry for invasion by environmental pyogenic bacteria (e.g., *Staphylococcus* and *Streptococcus* spp.), secondary pyogenic sepsis could have ensued [134,135]. It should be mentioned that in the four aforementioned cases (**KD41**, **KD520**, **KK61**, and **HC81**), even the customary use of the insensitive feet in standing and walking could have resulted in their plantar ulceration, particularly in the weight-bearing areas [72,134]. After the loss of cutaneous sensation, deep tissue sensation could have been preserved for a long time in the feet of **KD41**, **KD520**, **KK61**, and **HC81** [134]. Nevertheless, in later stages of the disease, the pathological process could have progressed gradually, distoproximally along the cutaneous sensory nerve fibres to the larger parent nerve trunks of the posterior tibial nerve, which contain not only sensory but also motor nerve fibres [172,174]. The subsequent regional sensory and motor dysfunction of these nerve trunks could have led to deep tissue anaesthesia and muscle paralysis, respectively [172–174]. Following the loss of deep tissue sensation in the feet of **KD41**, **KD520**, **KK61**, and **HC81**, there could have been extension of the pyogenic sepsis from the superficial tissues to the deep soft tissues, bones, and joint cavities, with consequent development of pyogenic septic periostitis, osteomyelitis, and/or arthritis, which could have given rise to the formation of the observed septic bony changes (e.g., surface pitting, subperiosteal new bone formations, and partial absorption) [69,131,134,135]. These skeletal lesions serve as direct evidence for the *in vivo* presence of plantar ulceration in the feet of **KD41**, **KD520**, **KK61**, and **HC81** [134]. In three out of these four cases (**KD41**, **KD520**, and **KK61**), the presence of alterations not only on the plantar but also the dorsal surface of the metatarsals implies that both foot surfaces could have been simultaneously affected by ulcers (Table 3). It is important to note that the same conclusions cannot be drawn for the feet of **HC81**: 1) in the left foot, the *post-mortem* missing of all of its bones precluded their evaluation, and 2) in the right foot, only the medial surface of the right calcaneus revealed septic bony changes, but the majority of the right foot bones were missing or severely damaged *post-mortem* (Table 2). In two other cases (**KD271** and **SS214**), where the foot bones did not provide any skeletal evidence for the presence of sensory impairment in the posterior tibial nerve (Table 3), its motor or autonomic dysfunction, which can be presumed in both feet of **KD271** and **SS214**, can indirectly indicate it. This is because loss of sensation is always accompanied by autonomic impairment and generally precedes motor dysfunction [34,134]. For the same reason, there could have been sensory neuropathy of the ulnar nerve in both hands of **KD41** and **KD271**, and at least the right hand of **SS214**. All of the six individuals with sensory impairment in the posterior tibial nerve (**KD41**, **KD271**, **KD520**, **KK61**, **HC81**, and **SS214**) revealed signs of periostitis (i.e., inflammation of the periosteum) on the tibiae and/or fibulae – in the form of surface pitting and longitudinally striated subperiosteal new bone formations, which were particularly located in the distal half or two-thirds of the affected shafts (Table 3) [71,72,134,135,154]. The presence of these inflammatory alterations suggests that the pyogenic infection could have ascended from the plantar ulcers of the feet to the long tubular bones of the lower legs of **KD41**, **KD271**, **KD520**, **KK61**, **HC81**, and **SS214** [134,135,154]. It is important to note that in **SS214**, the *post-mortem* missing of the left tibia and fibula precluded the evaluation of these bones for signs of periostitis (Table 2). In two cases (**KD271** and **SS214**), where there was no skeletal evidence of the *in vivo* presence of plantar ulcers (Table 3), the inflammatory bony changes detected in the lower leg bones could have resulted from a pyogenic infection that ascended from one or more plantar ulcers to the tibiae and fibulae before the pathological process could have involved the foot bones underlying the affected soft tissues [134]. In three individuals (**KD41**, **KD271**, and **KK61**), besides the periosteum of the lower leg bones, the crural interosseous membrane (i.e., a ligamentous structure, which connects the corresponding tibia and fibula throughout the length of their shaft) could have also become inflamed due to the pyogenic infection [135]. This could have given rise to the ossification of this ligamentous structure, with subsequent formation of the observed exostoses at its attachment sites on the adjoining tibia and fibula in both lower limbs of **KD41**, **KD271**, and **KK61** (Table 3) [135].

In four out of the six cases with postcranial bony changes (**KD41**, **KD271**, **KK61**, and **SS214**), the hand and/or foot bones provided direct evidence for the loss of motor function in the ulnar and/or posterior tibial nerves, respectively (Table 3). In two out of these four individuals (**KD271** and **SS214**), leprous impairment of the motor component of the ulnar nerve could have given rise to progressive paralysis of the flexor and extensor muscles of the hand with secondary hyperflexion of the interphalangeal joints and hyperextension of the metacarpophalangeal joints, which could have resulted in the development of 'claw-hand' deformity in both upper limbs of **KD271** and at least the right upper limb of **SS214** [13,154,174,175]. It is important to note that in the left hand of **SS214**, the missing of the phalanges precluded their definitive observation; and thus, the evaluation of the presence of claw-hand deformity (Table 2). In the proximal interphalangeal joints of **KD271** and **SS214**, where the sustained hyperflexion is usually the most marked, the long-standing pressure exerted by the palmar edge of the middle phalangeal bases could have induced bone atrophy at the distal end of the adjoining proximal phalanges; and thus, the formation of a shallow, sharply defined groove across their palmar surface (in the juxta-articular area at the distal end) (Table 3) [72,131]. In **KD271**, the same aetiology could have led to the development of a smooth remodelled bevelling on the palmar edge of the middle phalangeal bases (Table 3) [72,131]. It seems that there was no lateral deviation in the involved proximal interphalangeal joints of **KD271** and **SS214** as the shallow grooves were present across the entire width of the palmar surface of the affected proximal phalanges [131]. On both sides of the proximal and/or middle phalangeal diaphyses of **KD271** and **SS214**, marginal palmar osteophytes were detected (Table 3), which were described as entheseal changes of the superficial finger flexor muscles; and thus, could refer to permanent contracture of the soft tissues in the hand [176,177]. It should be mentioned that in the early stages of claw-hand deformity, there is only soft-tissue contracture [72,131]. Based on the above, it cannot be excluded that in another case (**KD41**), which displayed the same marginal palmar osteophytes in both hands (Table 3), there was leprous dysfunction of the motor component of the ulnar nerve and secondary development of claw-hand deformity in both upper limbs, but the individual died before other bony changes could have occurred in the hand phalanges. On the other hand, the shallow palmar grooving at the distal end of the proximal phalanges and/or the slight broadening and flattening of the palmar edge of the middle phalangeal bases in **KD271** and **SS214** are consistent with long-standing claw-hand deformity prior to death [131]. In at least **KD271** and **SS214**, deformation of the hand(s) could have led to their disfigurement and deterioration of the hand functions (e.g., weakened grasp, grip, and pinch), which could have had an adverse effect on the ability of these individuals to carry out normal day-to-day activities [175,178,179].

In three cases (**KD41**, **KD271**, and **KK61**), leprous dysfunction of the motor component of the posterior tibial nerve could have resulted in progressive paralysis of the muscles responsible for the maintenance of the longitudinal arch integrity in the foot with subsequent collapse of the longitudinal arch, which could have led to the development of 'flat-foot' deformity in both lower limbs of **KD41**, **KD271**, and **KK61** [72,132]. In the deformed feet of these three individuals (**KD41**, **KD271**, and **KK61**), because of the changed and abnormal mechanical stress between the tarsal bones, there could have been dynamic, progressive, plantar displacement of the navicular bones, which in turn could have imposed tensile stress on the dorsal tarsal ligaments [72,132]. This chronic ligamentous stress could have stimulated the formation of the exostoses (i.e., irregular, smooth ridges of new bone), which were observed at the attachment sites of the aforementioned ligaments on the dorsal surface of the tarsal bones (Table 3) [72,132,154]. In **KD41**, **KD271**, and **KK61**, deformation of the feet could have resulted in their disfigurement and difficulties in standing and walking; and thus, in conducting domestic and occupational physical activities [180].

In all of the six individuals with postcranial bony changes (**KD41**, **KD271**, **KD520**, **KK61**, **HC81**, and **SS214**), the hand and/or foot bones provided direct or indirect evidence for the loss of autonomic function in the ulnar and/or posterior tibial nerves, respectively (Table 3). In two out of these six cases (**KD520** and **SS214**), leprous dysfunction of the autonomic peripheral nerves innervating the foot could have given rise to circulatory disturbances with subsequent changes in the blood oxygen tension, which could have led to slow, progressive, concentric diaphyseal atrophy/remodelling of at least some of the metatarsals and/or phalanges in both feet of **KD520** and **SS214** by selectively stimulating regional extracortical osteoclastic and endosteal osteoblastic activity (Table 3) [69,70,133,154]. It is important to note that in the left foot of **KD520**, only two metatarsals were available for evaluation (the other foot bones were missing *post-mortem*), which did not show the aforementioned alteration type (Table 2). Nevertheless, it is permissible to infer that there was autonomic peripheral neuropathy not only in the right but also the left foot of **KD520**, as it is an invariable accompaniment of impaired cutaneous and/or deep tissue sensation, of which the presence can be presumed in both lower limbs of **KD520** [134]. A proximal phalanx of **KD520** represented the true pan-circumferential concentric type (remodelling in all diameters), whereas the metatarsals of **KD520** and **SS214** the knife-edge type (solely mediolateral remodelling) of concentric diaphyseal atrophy (Table 3). In both **KD520** and **SS214**, the progressive diaphyseal atrophy of at least some of the metatarsals and/or phalanges could have resulted in deformation of both feet with their consequent disfigurement; furthermore, these two individuals (**KD520** and **SS214**) would have experienced disability in performing the basic activities of daily living [70]. It should be mentioned that loss of the autonomic function in the small cutaneous nerve fibres of the foot could have led to impaired or diminished sweat-gland function in the anaesthetic skin patches in both lower limbs of **KD520** and **SS214**, with the anhidrotic skin becoming xerotic and hyperkeratotic [34,181,182]. As a consequence, the affected foot skin of these two individuals (**KD520** and **SS214**) could have more readily cracked even with normal usage; and thus, could have become even more susceptible to ulceration and secondary pyogenic infections [181,182]. On the other hand, due to damage to the vascular autonomic innervation, there could have been loss of vascular tone and secondary stasis of the capillary blood flow in the anaesthetic skin patches in both lower limbs of **KD520** and **SS214**, which could have resulted in impaired and delayed healing of ulceration [181,182]. Today, non-healing plantar ulcers are a common cause of disability and consequently, of reduced quality of life in patients with HD [44,183]. In the four other cases with postcranial bony changes (**KD41**, **KD271**, **KK61**, and **HC81**), where there was no skeletal evidence of autonomic nerve impairment in the hands and/or feet, the presence of autonomic peripheral neuropathy can be presumed in both feet (and maybe both hands) of **KD41**, both feet and hands of **KD271**, both feet of **KK61**, and at least the right foot of **HC81**. This is because in the hand and/or foot bones of these individuals, the presence of skeletal lesions (Table 3) suggestive of sensory and/or motor dysfunction of the ulnar and/or posterior tibial nerves indirectly indicate it, as loss of sensation is always accompanied by autonomic impairment and generally precedes motor dysfunction [34,134]. For the same reason, in **SS214**, there could have been autonomic peripheral neuropathy not only in both feet but also at least the right hand.

4.2. Social aspects

Although internal written sources are not available from the Avar-period Carpathian Basin, archaeological (burial) evidence can shed some light on how leprosy could have affected the life of the eight examined individuals and how they could have been perceived by other members of their communities. As all the four cemeteries from where the presented cases derive (Kiskundorozsma–Daruhalom-dűlő II, Kiskundorozsma–Kettőshatár I, Hajós-Cifrahegy, and Sükösd-Ságod) are unpublished and their detailed archaeological analysis is still ongoing, a nuanced comparative analysis is limited, but some general observations

can be made.

All of the eight examined individuals (**KD41**, **KD119**, **KD271**, **KD518**, **KD520**, **KK61**, **HC81**, and **SS214**) were buried together with other members of their communities, in the same cemeteries. Since the exact prevalence of the disease in these communities is impossible to be assessed, possibilities of a spatial analysis are restricted, but the burials of individuals with leprosy fit into the structure of the cemeteries, do not form separate clusters, and when they are located near the edges of the cemeteries, it is the result of the organic chronological development of the sites. The lack of spatial separation of recognisably ill individuals is interesting, as spatial and social segregation is a natural reaction to disease in many communities. Today, when most mechanisms behind the transmission of various infectious diseases are known, this separation serves to prevent larger epidemics. As attested by the written sources, this idea of halting or slowing down the spread of diseases by segregating those who fell ill was already known and actively practiced for hundreds of years in mediaeval Europe. It is hard to find an example where the role of this segregation is more prominent and conspicuous than in the case of leprosy. In the High Middle Ages (after the 11th century CE), numerous, mostly religious notions and ideas already existed about the nature and meaning of HD. However, it is less evident how leprosy was perceived during the early mediaeval period, i.e., between the 5th and 10th centuries CE, especially in geographical regions without any internal written sources, such as the Carpathian Basin during the Avar period.

Leprosy affects the life of its victims for a long time, in multiple ways. In the past, this could have led to the emergence of various HD-related identities, be they positives or negatives, that defined social norms and behaviours between leprosy sufferers and other members of the community. On the one hand, HD could have heavily limited or changed an individual's possibilities to engage and participate in social acts, which has important roles in creating or reinforcing a sense of sameness and communal identity or existing social structures between participants; thus, forming a community. In most severe cases, the disease and its complications could have rendered an individual incapable of self-sufficiency. On the other hand, physical disabilities or deformities, especially on the face, could have heavily influenced an individual's role and standing in the community. The irreversible changes in the physical appearance and mobility resulting from leprosy could have reduced the quality of life of all the eight examined individuals. In the milder or moderate cases (**KD41**, **KD119**, **KD518**, **KD520**, and **SS214**), it probably meant nerve impairment in the limbs with some deterioration in the hand and/or foot functions (e.g., clumsiness). This would have had an adverse effect on the ability of these individuals to carry out certain physical activities (e.g., grasping or walking); and thus, would have excluded them from some of the normal day-to-day activities. In addition, the impaired nasal breathing, the aesthetic repercussions (e.g., facial disfigurement) due to at least soft-tissue lesions, as well as the unpleasant body odour due to foul-smelling nasal discharges and/or halitosis would have been disadvantageous for them in social situations [184]. Nevertheless, the aforementioned individuals (**KD41**, **KD119**, **KD518**, **KD520**, and **SS214**) would have still been able to look after themselves. On the other hand, in the most severe cases (**KD271**, **KK61**, and **HC81**), the very serious physical sequelae of HD (i.e., severe deformity of the rhinomaxillary region, feet and/or hands with associated disability) would have made these individuals incapable of self-sufficiency or active participation in most social situations. They would have required continuous support from their families and/or communities.

Despite this, we do not see any evidence of a 'social stigma' in their mortuary treatment. All of the evaluated graves are pit-graves with occasional ledges (**KD41**, **KD119**, and **KK61**), coffins (**KD119**, **KD71**, **KD518**, **KD520**, and **SS214**), and funerary beds (**KD119**, **KD520**, and **KK61**) – all of these are fairly common at the aforementioned sites (Table 1 and Supplementary texts 1–4). One exception is the posthole structure of the burial of **KD41** (an adult male from the Kiskundorozsma–Daruhalom-dűlő II site), which suggests a more elaborate grave construction (Table 1). In terms of size, compared to the averages of the respective cemeteries, there are both relatively large (**KD41**, **KD119**, and **KK61**) and relatively small (**HC81**) graves (Table 1 and Supplementary texts 1–4). Their orientation corresponds to the dominant orientation (Table 1 and Supplementary texts 1–4). Most of the evaluated burials contained only domestic artefacts, such as knives and spindle-whorls (**KD41**, **KD271**, **KD518**, **KD520**, **KK61**, and **SS214**), or very simple dress accessories, such as iron belt buckles (**KD41**, **KD271**, **KD518**, **KK61**, and **SS214**), and animal remains interpreted as food offerings (**KD41**, **KD119**, **KD271**, **KD520**, **KK61**, and **HC81**) – all of these are fairly common interments in the above-mentioned sites (Table 1 and Supplementary texts 1–4). Again, the one exception is **KD41**, who was buried with a set of copper-alloy mounts, a strap-end belonging to a belt, and a copper-alloy earring (Table 1). The presence of an elaborate belt set is generally interpreted as an artefact representing higher social status [185,186]. In most of the examined individuals (**KD41**, **KD119**, **KD271**, **KD518**, **KD520**, **KK61**, and **SS214**), the disease could have become apparent during adulthood, at a point of their life when their social position in their communities have been already established. It might have been deteriorated due to HD, but the relatively richly furnished burial of **KD41** (Table 1) suggests that there was also a possibility to maintain it. **HC81**, a juvenile (16–18 years old) girl from the Hajós–Cifrahegy site, is an exception as she could have started to manifest signs and symptoms of leprosy in childhood. It cannot be excluded that the complications of HD contributed to the early death of **HC81** and probably defined her whole life. In the Avar-period Carpathian Basin, young females between 16 and 20 years of age tend to be buried in the most richly furnished graves as a result of their high 'value' as they became fertile and available for marriage [187]. (It should be mentioned that a similar tendency was observed in the 6th-century-CE Carpathian Basin [188], as well.) It seems that **HC81** was buried without any grave goods in a relatively small grave (Table 1), but it is impossible to declare for certain that it was solely HD and its complications that could have been responsible for the observed mortuary treatment.

The lack of segregation of leprosy sufferers in the four Avar-period cemeteries from where the presented cases derive is not unique in the early mediaeval period. Although the archaeological evidence is generally scarce, in a 10th–11th-century-CE cemetery excavated in Norwich, 13.3% of the deceased (~30% of the well-preserved skeletons) were diagnosed with HD [189] – they were buried together with other members of the community. There is also evidence for the opposite: at Winchester, two burials dated to ca. 700 CE were found in the ditch outside the wall; one of the individuals exhibited signs of HD and was buried on their side [190]. These two examples also highlight one of the limitations of burial archaeology: sufferers of leprosy buried together with the rest of the community are much easier to be identified as they are part of a larger site, but individuals buried in a separate location are rarely found and often lack wider context. The so-called leper houses (leprosaria) or colonies, for long considered as places for segregation, now viewed also as places for institutionalised care, support, and integration [55], documented from the 5th century CE onwards in Western Europe [191] were mainly religious institutions. A similar concept also appeared in the Islamic world as early as the 8th century CE [192]. In the Avar-period Danube-Tisza Interfluve, such solutions did not play a role, but based on the evidence provided by the four sites from where the presented cases derive, especially the Kiskundorozsma–Daruhalom-dűlő II cemetery with a relatively high number of individuals with HD, these rural communities provided and cared for the ill and maintained a strong enough social network that made the survival of leprosy sufferers possible even after becoming incapable of self-sufficiency.

5. Conclusions

In recent years, our knowledge and understanding of how society

viewed HD and treated its victims in the past has substantially been enriched due to collaboration between researchers from different disciplines (e.g., history and bioarchaeology). Nonetheless, most studies focus their attention on Europe during the High and Later Middle Ages, and are based on written sources created in Christian environments. Therefore, much still remains to be discovered, especially in geographical regions and archaeological periods where internal written sources are scarce or not available at all, such as the Avar-period Carpathian Basin. In these instances, burial evidence can shed some light on how leprosy was perceived. By providing the comparative analysis of eight Avar-period HD cases from the Danube-Tisza Interfluve (Hungary), the core territory of the Avar Khaganate, our paper contributes to fill in some of the aforementioned gaps, as it gives us a unique insight into the biological consequences of living with leprosy and illustrates the social attitude toward the afflicted in the four Avar-period rural communities from where the presented individuals derive. Based on our results, in every case, the dermatological, neurological, and orthopaedic complications of the disease led to irreversible changes in the patient's physical appearance and mobility. These would have been disadvantageous for them and limited or changed their possibilities to participate in social situations. Although the milder or moderate cases would have still been able to look after themselves, the most severe cases, who would have been incapable of self-sufficiency or active participation in most social situations, would have required continuous support from others to survive. Despite the very visible disease and associated debility of the eight examined individuals, there seems to be no evidence of a 'social stigma' in their mortuary treatment: they were buried together with other members of their community, in the same cemeteries. In addition, their graves conformed to the mortuary practices characteristic of the four cemeteries (Kiskundorozsma–Daruhalom-dűlő II, Kiskundorozsma–Kettőshatár I, Hajós–Cifrahegy, and Sükösd–Ságod) they were buried in (e.g., construction and orientation of the grave, and type and quantity of accompanying grave goods). Although distinction or segregation in life do not preclude normative treatment in death, the long-lasting survival of the examined individuals with HD, especially the most severe cases, implies that they would not have been abandoned but cared for by others. Our study expands and improves our knowledge and understanding of not only leprosy, but also the disease experience by both those afflicted with HD and society at large during the early mediaeval period, when treatment was not an option for the victims; and thus, the disease could have developed in its natural course, eventually leading to severe physical disfigurement and impairments, and associated social consequences. In the future, palaeogenomic analyses of mycobacterial and human aDNA remains deriving from osteoarchaeological series, like the cases included in the current paper, will be able to give more insights into the past of HD. For instance, they can provide us with invaluable information about the origins and geographical distribution of leprosy bacilli, and the migration routes of their human host over time.

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Author contribution statement

Olga Spekker: Conceptualisation, Methodology, Investigation, Data curation, Writing – Original draft preparation, Writing – Review & Editing, Visualisation, Project administration; Balázs Tihanyi: Investigation, Visualisation; Luca Kis: Visualisation; Ágota Madai: Investigation, Visualisation; György Pálfi: Resources; Erika Wicker: Investigation, Visualisation; Réka Csuvár-Andrási: Visualisation; Csaba Szalontai: Investigation, Visualisation; Levente Samu: Writing – Original draft preparation, Visualisation; István Koncz: Writing – Original draft preparation; Antónia Marcsik: Investigation, Supervision; Erika Molnár: Investigation, Supervision.

Declaration of competing interest

None.

Appendix A. Supplementary data

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