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REVIEW

Paget's Disease of Bone among Various Ethnic Groups

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مرض باجيت (Paget's Disease) الذي يصيب العظام ضمن المجموعات العرقية المختلفة

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ABSTRACT: Paget's disease of bone (PDB) is a relatively benign disease common among many European populations, including those in the UK, Italy and Spain. However, it appears to be rare among Scandinavians and non-European immigrants living in Europe. The prevalence among Asian populations may be underestimated because a large number of reported cases were discovered incidentally. There is a need for surveys addressing the prevalence rate and consequences of PDB to be carried out in various parts of the world, particularly Asia.

Keywords: Paget's Disease of Bone; Ethnic Groups; Epidemiology.

الملخص: يعد مرض باجيت الذي يصيب العظام (PDB) من الأمرض الحميدة نسبياً وهو شائع بين سكان المناطق الأوروبية، ومن ضمنها سكان المملكة المتحدة وإيطاليا وإسبانيا. ومع ذلك فهو نادراً ما يظهر بين الاسكندنافيين والمهاجرين من أصول غير أوروبية الذين يعيشون في أوروبا. وقد يكون تقدير انتشار هذا المرض بين سكان آسيا أقل كثيرا مما هو في الواقع بسبب أن عددا كبيرا من الحالات المسجلة كان اكتشافها مصادفة. إن هنالك حاجة لإجراء دراسات استقصائية لدراسة معدل انتشار ونتائج الإصابة بمرض باجيت التي لا بد من معرفتها والأخذ بها في أجزاء مختلفة من العالم، وخاصة آسيا.

مفتاح الكلمات: مرض باجيت الذي يصيب العظام؛ المجموعات العرقية؛ علم الأوبئة.

Paget's disease of bone (PDB) is characterised by the disruption of bone formation and resorption which leads to bone deformities. It is considered to be a relatively benign bone disease in most cases. The most commonly affected sites are the pelvis [Figure 1], femur, tibia, lumbar spine and skull; thus, abdominal radiographs are often performed to diagnose PDB in people over the age of 55 years.[1] The disease is more prevalent among northern European populations, including Scandinavians, and is considered to be uncommon in non-Caucasians.[1] Randomised trials have shown that antiresorptive therapy decreases bone pain and lowers alkaline phosphatase levels, which helps to assess the extent and severity of the disease in affected patients.[2]

The aetiology of PDB is not yet fully understood. However, genetics are thought to play a part in the disease's development, with more than 20% of PDB patients reporting a first-degree relative with the same condition.[3] Studies have shown the involvement of specific genetic *loci*, including the *colony stimulating factor 1*, *optineurin*, *transmembrane 7 superfamily member 4* and *Ras and Rab interactor 3* genes.[3,4] Heterozygous mutations affecting the *sequestosome 1* (*SQSTM1*) gene, which are clustered in the ubiquitin-binding domain encoded by exon 7 and 8, have been commonly reported among PDB patients.[5] The other type of mutation is less common and includes domain-specific defects within valosin-containing protein which can lead to PDB in a rare syndrome associated with dementia and late-onset inclusion body myopathy.[6] A viral aetiology remains controversial, since these observations have not always been replicated and thus far, viruses have not been isolated from pagetoid tissue.[7]

As the prevalence of PDB has decreased in certain countries over the past 25 years, it has been suggested that environmental factors may be important in the development of PDB.[8] However, additional research addressing the environmental impact on the development of PDB is required. The highest prevalences of PDB are found in Britain, Australia, New Zealand, North America, western Europe and among Caucasians over the age of 50 years.[9,10]

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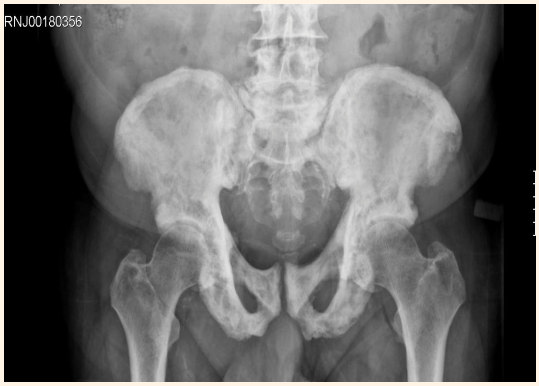

Figure 1: Radiograph of the pelvis of a 73-year-old patient originally from Sierra Leone with widespread Paget's disease of the bone.

Prevalence in Various Regions

EUROPE

PDB is common in Caucasians, although the disease rarely occurs among individuals below 50 years old.[1] It has been found that the rate of PDB increases significantly in those over 90 years of age.[11] Within the UK, the prevalence of this condition appears to have decreased over recent years. In a study conducted in 1980, it was found that the north-western Lancashire towns of Preston, Bolton, Wigan, Burnley and Blackburn had an average PDB prevalence of 6.8%, while Lancaster had the highest prevalence rate at 8.3%.[12] However, a more recent study conducted in England and Wales revealed a total prevalence of 0.3% among men and women aged 55 years and above.[13] This suggests a dramatic decline in the PDB prevalence in the UK.

Table 1: Age- and sex-standardised prevalence of Paget's disease of bone among hospital patients aged ≥55 years in various European towns[16]

Town	Prevalence in %
UK*	4.6
Bordeaux, France	2.7
Rennes, France	2.4
Nancy, France	2.0
Dublin, Ireland	1.7
Valencia, Spain	1.3
Essen, Germany	1.3
Palermo, Italy	1.0
Porto, Portugal	0.9
Galloway, Ireland	0.7
Athens, Greece	0.5
Crete, Greece	0.5
Malmo, Sweden	0.4

**Prevalence calculated from 31 towns in the UK.*

Table 2: Age-standardised prevalence of Paget's disease of bone in African-American and Caucasian residents in two cities in the USA[20]

City	Ethnic group	Prevalence in %		
		Men	Women	Both
New York	African	3.3	2.0	2.6
New York	Caucasian	5.2	2.5	3.9
Atlanta	African	1.9	0.6	1.2
Atlanta	Caucasian	0.9	0.8	0.9

Although this disease is generally not seen in non-European populations, a case series reported eight non-Caucasian PDB patients in East London in the UK.[14] Two of the patients were of Bangladeshi origin and both died of complications; one had an angiosarcoma and the other had an osteosarcoma. Both patients were male and relatively young (63 and 58 years old).[15]

Similar PDB prevalence rates were found in a survey of 13 different European towns across nine countries (2–3%), except for Sweden which showed a much lower prevalence (0.4%) [Table 1].[16] In Italy, the overall rate of PDB was found to range between 0.7–2.4%.[17] A recent study demonstrated that the incidence of PDB in two regions of Spain had stayed the same over the past 24 years, although the severity of the disease had declined.[18] Campagnia, Italy, and Vitigudino, Spain, are also known to have a high prevalence of PDB.[19]

NORTH AMERICA

In the USA, approximately 1% of the population are affected by PDB, with the north-eastern region of the USA showing the highest prevalence.[20] Although the disease is thought to be rare in non-Caucasian populations, research has indicated that there is no difference in prevalence between Caucasians and African-Americans.[21] A survey carried out in New York City, New York, and Atlanta, Georgia, revealed that while there was a different prevalence between the two cities, there was a similar prevalence between the two ethnic groups [Table 2].[20]

AUSTRALIA AND NEW ZEALAND

PDB is also common in Australia and New Zealand, with a prevalence of approximately 4%.[21,22] In one study, the prevalence was found to be higher among British migrants coming to Australia than among the Australian residents.[21] Recent evidence suggests a decrease in the prevalence rate and severity of the disease in New Zealand.[22] A study of the Asian population in Auckland, New Zealand, showed nearly the same prevalence of PDB as in people of European origin.[23] This finding suggests that the low prevalence

of PDB in Asia, as discussed later on in this review, might be underestimated due to a lack of awareness among physicians.

AFRICA

PDB is also common in South Africa. A survey of abdominal radiographs from 1,003 South Africans of European descent and 1,355 South Africans of African descent who were 55 years or older, showed prevalence rates of 2.4% and 1.3%, respectively.[24] The disease prevalence varies in other regions of Africa; however, it is generally rare. A study of 82,000 radiographs collected over four years in Freetown, Sierra Leone, revealed only 14 cases of PDB, while no documented case was detected over the same period and number of radiographs in northern Nigeria.[25] Research has shown that this disease is also rare in sub-Saharan Africa.[25]

ASIA

In Asia, PDB is known to be rare; however, there are reported cases among Chinese patients.[26–28] In Singapore, five cases of PDB were found over an eight-year period.[29] This series included a 72-year-old Indian patient whose diagnosis of PDB was made incidentally after he had suffered an ischaemic stroke. A computed tomography scan of the head revealed bony changes in the skull consistent with PDB and his serum alkaline phosphatase levels were also elevated.[29] There have been other reported cases of PDB among Indians, although its true prevalence in the Indian population is suspected to be higher, as most cases are discovered incidentally.[30,31]

As mentioned previously, research has indicated a similar prevalence of PDB between individuals of Asian and those of European origin,[23] indicating that this disease is under-recognised in Asia. Furthermore, a review of PDB among the ethnic Thai population theorised that the prevalence of this disorder will increase in the future due to the increasing number of Asian-European intermarriages.[32] Thus, it is imperative that healthcare workers in Asia increase their awareness of PDB and its symptoms in order to provide effective care for their patients.

SOUTH AMERICA

In South America, PDB is generally present among those of European descent, with research demonstrating that the disease is not present within the indigenous population.[33] The incidence is relatively high in Argentina, especially around Buenos Aires, which has a large population of Spanish and Italian immigrants. It occurs less frequently in Chile and Venezuela, both of which have fewer citizens of European descent.[33] However, a pilot epidemiological study conducted in the city of Recife, in north-east Brazil, found a similar PDB prevalence (6.8 per 1,000 people) and incidence (50.3 per 10,000 person-years) as that noted in southern Europe.[34]

THE MIDDLE EAST

A survey conducted in southern Israel from 1968–1993 yielded 61 cases of PDB and indicated a prevalence of approximately 1%, which is close to that found in southern Europe.[35] The majority of these cases were patients of Afro-Asian descent (56%), with the remaining 44% of Afro-Asian origin. Israel was the country of origin for few of the identified PDB patients; Romania, Tunisia, Australia and Argentina were the most frequent countries of origin. All of the patients were Jewish with the exception of one Bedouin Arab.[35] In another study carried out between 1961 and 1985 in four medical centres in Israel, 278 cases of PDB were identified in Jewish patients.[36] Only six of these patients were immigrants, of which 74% were originally from Eastern Europe. There were no patients of Arab ethnicity included in the 278 studied PDB cases.[36]

There have been isolated cases of PDB reported in Saudi Arabia, Iran, Iraq and Turkey.[37–40] Although, to the best of the authors' knowledge, no cases of PDB in Egypt, Lebanon or Syria have been published, there are verbal reports from rheumatologists in these countries about isolated cases of PDB in the local Arab populations.

Recommendations for Future Research

It is difficult to be certain of the exact prevalence of PDB among various ethnic groups due to the small sample sizes used in many studies. Based on the available research, PDB appears to be comparatively rare in Asian and African populations. However, it is very likely that this disease is under-reported in these populations, especially given the lack of prevalence studies in Asian and African countries. There is no clear explanation for the high PDB prevalence in Lancashire, UK, but the fact that this area has a high proportion of immigrants who are Asian in origin may be significant.[12] Therefore, there is a need to conduct epidemiological studies aimed at estimating the prevalence of the disease among Asians and Caucasians. Further studies should seek to investigate the true prevalence and incidence of PDB in various regions of the world.

The overall prevalence of this disease has decreased by 36% over the last 19 years.[41] This decline

is mostly attributed to environmental rather than genetic factors.[41] However, while significant progress has been made in the identification of the exact genetic mutations associated with PDB, further research is needed to determine the precise environmental factors involved.

Conclusion

PDB appears to be more common among Europeans and rare among Asian and African populations. However, cases of PDB in Africa and Asia are likely under-reported, resulting in a need for further epidemiological studies to assess the true incidence of this disease in both Caucasian and non-Caucasian populations. Considerable progress has been made regarding the genetic factors associated with PDB. However, it is theorised that environmental factors contribute greatly to the development of this condition. Future research is therefore recommended in this area.

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