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New cases of rare genetic disorder identified

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Scientists at the University of Liverpool, working with international partners, have shown a rare genetic disease, that causes crippling osteoarthritis in the spine and major joints, is far more prevalent worldwide than previously thought.

Researchers have identified more than 100 new cases of the disease, called alkaptonuria (AKU) in a small community in Vellore, India, bringing the total number of patients there to 130. Approximately 40 patients have been found in a village in Southern Jordan, but previously the disease had been unknown to healthcare workers in the region. There were only four known cases in the UK in 2003, but this has since risen to more than 80 patients across the country.

Research findings suggest that more work is needed to raise the profile of the disease in countries around the world so that it can be correctly identified by medics. It is thought to affect one in 250,000 people worldwide, but many remain undiagnosed or misdiagnosed as osteoarthritis.

Scientists at Liverpool are bringing international researchers together as part of the AKU Society to establish a global network that will help further understanding of the condition within communities and healthcare practices. The AKU Society was established in Liverpool in 2003 and supports patients diagnosed with the disease.

Patients being treated for AKU do not have enough of the enzyme, homogentisic acid oxidase, which causes acid to build up in the body.

Some of this acid is eliminated in the urine, but the remainder is deposited in body tissue where it is toxic. As a result, a black pigment, called ochronosis, forms and binds to bone, cartilage and skin. This can cause erosion of the cartilage and patients often have to undergo joint replacement surgery.

Dr Lakshminarayan Ranganath, researcher at the University's Institute of Ageing and Chronic Disease and clinician at the Royal Liverpool University Hospital, said: "AKU was the first genetic disease to be identified by scientists. It was described in 1902 by an English physician, but more than 100 years later there is still no cure for the disease. A drug candidate has recently been identified and is awaiting clinical trials to see if it could be used to treat AKU patients. We want to identify as many people with the condition as possible to ensure these important trials go ahead.

"Recent findings in India and Jordan show us that this disease is more prevalent than current statistics suggest and we urgently need to get research out into healthcare practices around the world so that cases can be identified and diagnosed correctly. We want to expand our international links as well as promote PhD opportunities to young researchers looking to progress our knowledge of the disease.

Professor James Gallagher, AKU researcher at the University's Institute of Ageing and Chronic Disease, said: "We are currently working to understand why the black pigment that attaches itself to joint cartilage only attaches to certain areas, whilst other sections of cartilage remain pigment-free. If we can understand the mechanisms of how the pigment binds in the body then we may be able to prevent the disease developing."

Isaac Jebaraj, Professor of Orthopaedic Surgery at the Christian Medical College, Vellore, India, said: "My work is focused on a Romani

Community in South India, where we have identified approximately 100 cases of AKU. It is important for us to reach these communities as traditionally they do not attend hospitals for aliments, preferring to use herbs and oils instead. As such we anticipate that there are many more people in India with this condition that have yet to be diagnosed with the condition.

"We have now treated many of the community with anti-inflammatory drugs and some have had surgery for joint replacement. To ensure that potential new treatments reach these communities, it is important that scientists work together to progress with drug trials."

Provided by University of Liverpool