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Digital Analysis of Clinical Screening Criteria for a Rare Disease - Behcet's Disease

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Abstract. The objective is to identify clinical screening criteria for a rare disease,- Behcet's disease and to analyse the digitally structured and unstructured components of the Identified Clinical criteria, build a clinical archetype using OpenEHR editor to be used by learning health support systems for clinical screening of the disease. Methods/Search Strategy: Literature search was conducted, 230 papers were screened, and finally 5 papers were retained, analysed and summarised. Digital Analysis of the clinical criteria was done and a sandardised clinical knowledge model of the same was built using OpenEHR editor, underpinned by OpenEHR international standards. Results The structured and unstructured components of the criteria analysed to be able to incorporate them in a learning health system to screen patients for Behcet's disease. SNOMED CT and Read codes were assigned to the structured componenets. Possible misdiagnosis were identified, along with their corresponding clinical terminology codes that can be incorporated in the Electronic Health Record systems. Conclusion: The identified clinical screening was digitally analysed which can be embedded into a clinical decision support system that can be plugged onto the primary care systems to give an alert to the clinicians if a patient needs to be screened for a rare disease, for e.g., Behcet's.

Keywords. Behcet's disease, rare disease, clinical screening criteria, EHR

1. Introduction

Clinical Screening of Rare Diseases: There are around 7,000 conditions that occur in <1/2000 populations and classified as rare diseases [1]. Diagnosis is often delayed, with consequent impact on avoidable costs, mostly due to unnecessary consultations, referrals and clinical investigations. Many organisations are trying to build algorithms called diagnostic criteria and use large databases of primary care Electronic Medical Records (EMRs) to identify patients that would meet these diagnostic criteria early.
Behcet's disease: In this study, we have chosen Behçet's disease (BD) a rare vasculitic disorder, characterized by a triple symptom complex of recurrent oral aphthous ulcers, genital ulcers, and uveitis. The disease appears to involve an autoimmune response triggered by exposure to an infectious agent [2].
Objective: The challenge for clinicians is to even consider the possibility of diagnosis of a rare disease like BD and if they do, it's a challenge to have a clear way of

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summarising the screening criteria in a standardised and computational way so they can weight up the likelihood formally. The objective of this paper is to identify clinical screening criteria for a rare disease- BD, and to digitally analyse it into its its structured and unstructured components, build a formal clinical archetype using OpenEHR editor [3] that can be used by learning health support systems for clinical screening of BD.

2. Methods

Searches were conducted in PubMed, Google Scholar, Cochrane Library, Embase, *Clinicaltrials.gov. Over 230 papers were screened and filtered based on duplicates, then by reading the titles 60 were shortlisted and based on their abstracts 9 papers were retained. Based on full text, 5 papers were finally retained analysed and summarised. Papers were included if international criteria for clinical screening and/or diagnosis of BD was studied or compared. Keywords used: Behcet's disease , Criteria, Clinical, Screening, Diagnosis. Clear and evidence-based criteria for the clinical screening of BD was used to digitise it for encoding into the EHR systems. The structured and unstructured components of the criteria were analysed. SNOMED CT and Read codes were assigned to the structured elements. Possible mis/differential diagnosis were identified [4] so that their corresponding terminology codes can be incorporated in the EHR systems. A sandardised clinical knowledge model was built using OpenEHR editor.

3. Results

Kiafer et al evaluated the referral Behçet clinics, and the alternative diagnoses established could be used as the list of the most common differential diagnoses for BD [4] International Study Group (ISG) clinical diagnostic criteria was simpler to use and had an improved screening performance than its predecessors [5]. Having realised its low sensitivity, an International Team for the Revision of the International Criteria BD (ICBD) (from 27 countries) led its reassessment. The new proposed criteria (ICBD) exhibits much improved sensitivity over the ISG criteria while maintaining reasonable specificity. For the ICBD, (refer to Figure 1) a patient scoring ≥4 points is classified as having BD and a score of ≥3 for indication of clinical screening [6].

In the training set, ICBD criteria showed 93.9% sensitivity and 92.1% specificity compared with 81.2% sensitivity and 95.9% specificity for the ISG criteria [4,5]. Adding 1 point for pathergy test increased the estimate of sensitivity for ICBD from 95.5% to 98.5%, while specificity was reduced from 92.1% to 91.6%. only [6].

Sign/symptom	Points
Ocular lesions	2
Genital aphthosis	2
Oral aphthosis	2
Skin lesions	1
Neurological manifestations	1
Vascular manifestations	1
Positive pathergy test*	1*

*Pathergy test is optional and the primary scoring system does not include pathergy testing. However, where pathergy testing is conducted one extra point may be assigned for a positive result.

Figure 1. ICBD point score system: score >=4 indicates Behcet's diagnosis and >=3 for clinical screening [6]

Davatchi et al [7] compared the performance of ISG and ICBD criteria, concluding that ICBD has better sensitivity (96.5%), and accuracy than ISG (83.7%) [7]. Sensitivity is more important and crucial in clinical screening criteria, especially when it's a rare disease, ICBD becomes the criteria of choice. With the wide use of EHR systems, the data is expected to be available in structured form. The unstructured data if required can be found with 'Natural language processing' tools. Here, the clinical knowledge was formally represented using the Ocean Informatics archetype editor, underpinned by OpenEHR EHR standards [3], to be incorporated into the primary and secondary EHR systems for the screening of BD.

Table 1. Analysis of the ICBD Screening Criteria components for BD for using with an EHR system

Clinical Features	Unstructured primary care records	Structured Primary care records: SNOMED CT Codes	Possible Misdiagnosis
Oral apthosis	Oral ulcer, Mouth ulcer, Ulcer on tongue, Ulcer of Mouth Canker Sores, Sore/s OR Ulcer/s	26284000 | Ulcer of mouth (disorder) | 1071000119107 | Oral lesion (finding) | 426965005 | Aphthous ulcer of mouth	**Simple aphthous lesions**
Genital apthosis	Penis ulcer,, Vulva* ulcer, Labial ulcer, Genital ulcer Sore/s OR Ulcer/s	95589007 | Ulcers of male genital organs	
Ocular lesions: **Anterior Uveitis** **Posterior Uveitis** **Retinal Vasculitis**	Eye pain, Occular pain Pain in eye Eye Redness Photophobia Uveitis Anterior Uveitis Posterior Uveitis Retinal Vasculitis	41652007 | Pain in eye 75705005 | Red eye 12241791000119109 | Bilateral red eyes 28473001|Uveitis 43363007 | Posterior uveitis 410692006 | Anterior uveitis	**9826008 | Conjunctivitis** **53726008 | Acute conjunctivitis**
Skin lesions: **Pseudofolliculitis,** **Skin aphthosis,** **Erythema nodosum**	Skin nodules, Itching and redness of skin Skin sore OR ulcer Pseudofolliculitis,	95319004 | Skin nodule (finding)	**4776004 | Lichen planus**

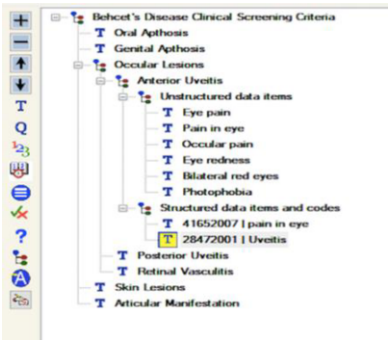

Figure 2. Clinical archetype of the ICBD clinical screening criteria for BD using OpenEHR editor

4. Discussion

One of the challenges is considering the possibility of such a rare disease diagnosis. The symptoms sometimes present in a piecemeal way and the clinicians capturing the individual symptoms don't put the pieces together and think of a rare disease like BD. The archetype represents a structured format for capturing data at a single encounter that would be useful for somebody who is thinking about the possibility of BD and now wants to formally walk through the screening criteria as an EHR template (modelled on the archetype built in Figure 2) in order to have a clear and complete picture of the existence of the diagnostic screening criteria, so one can then arrive at a decision. A second way in which this clinical screening archetype structure could be used is to construct an archetype-based query to examine EHRs that might have clinical features that form parts of this archetype captured at different dates and times but never brought together. This would enable the possibility of BD to be screened for patients for whom that diagnosis had not yet occurred as a possibility to the treating clinicians.

Challenges and limitations in implementing the proposed clinical archetype can be upgrading the EHR systems, training of IT staff and clinicians and the cost incurred. Strategies to engage the stakeholders and scale up to other rare diseases can be helpful.

5. Conclusion

The clinical screening criteria for a rare disease-Behcet's disease was successfully found through literature review and comparing the sensitivity and specificities of different international clinical screening criteria. The components of the criteria could be analysed into structured and unstructured data, terminology codes applied (including the codes for possible differential diagnosis) and the clinical knowledge could be formally represented and digitised to be incorporated into and to be used by EHR systems for screening BD. Similar approach can be applied to establish and incorporate the clinical screening criteria of other rare diseases into the primary EHR systems, with implications of early diagnosis and treatment, less complications and hosptalisations, better prognosis and thereby leading to improved quality of care for patients and cost savings.

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