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Hidradenitis suppurativa in a cohort of children and adolescents with overweight and obesity

Short title: HS in a childhood obesity cohort

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Tables: 2

The study was conducted in Denmark at The Children’s Obesity Clinic, Department of Paediatrics, Copenhagen University Hospital Holbæk and Department of Dermatology, Zealand University Hospital, Roskilde.

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Conflict of interests:
None
ABSTRACT

Background: Hidradenitis suppurativa (HS) is a chronic, inflammatory, and recurring disease, mainly observed in adults. Obesity is considered an important independent factor in HS development and is associated with a higher prevalence of HS in children. We aimed to characterize the clinical presentation of HS in children and adolescents with overweight or obesity.

Methods: We performed a cross-sectional observational study during January 2007 – April 2015. Patients with overweight and obesity (5-17 years of age, BMI > 90\textsuperscript{th} percentile) referred to The Children’s Obesity Clinic, Department of Paediatrics, Copenhagen University Hospital Holbæk, Denmark, underwent screening for dermatological conditions. A dermatologist ascertained the diagnosis of HS, and disease severity was assessed using Hurley staging and Sartorius score. Tobacco smoke exposure, body mass index (BMI) standard deviation score (SDS), and psychiatric comorbidities were recorded. Our cohort was compared with a reference cohort recruited in a previous study.

Results: A total of 195 children and adolescents underwent screening for dermatological conditions. Nine patients screened positive, and six of these patients were available for examination of whom five presented with HS. All HS cases were mild (median Sartorius score of 9). Four of the five patients (with varying constellations) reported tobacco exposure, a positive family history of HS, and exhibited psychiatric comorbidities.

Conclusion: Our findings support that the presence of pediatric HS is correlated with familial disposition to HS and psychiatric comorbidities.
Introduction

Hidradenitis suppurativa (HS) is a chronic, inflammatory, and often severe skin disease of the hair follicles affecting intertriginous areas. HS usually presents after puberty with painful, deep-seated, inflamed lesions in the apocrine gland-bearing areas of the body, most commonly the axillary, inguinal, and anogenital regions. The disease is recurrent with a minimum of two flares within six months or one or more chronic lesions lasting more than three months. (Dessau definition, 1st International Conference on Hidradenitis suppurativa/Acne inversa, March 30–April 1, 2006, Dessau, Germany)¹-³. Long-term follow-up suggests that approximately one-third of patients experience remission within a 25-year period⁴. The accompanying pain, discharge, and malodour may be associated with psychosocial comorbidities, social isolation, and consequently a reduction in quality of life⁵-⁹.

The aetiology and pathogenesis of HS are not fully clarified but have been suggested to include anatomical abnormalities of the hair follicle and inappropriate interactions between the host and its skin microbiota¹⁰. Inheritance, obesity, and smoking are considered important pathogenic factors in the development of HS². In particular, the degree of obesity is positively correlated with HS severity, and the prevalence of HS is higher in patients with obesity⁴,¹¹-¹³.

HS in children

Retrospective data suggest that the most common age at onset of HS is the early twenties⁴,¹⁴. It is further suggested that the development of pre-pubertal or pubertal HS may be a harbinger of more widespread disease compared with normal-onset HS¹⁵.

Early-onset HS is considered rare with a reported incidence of 2.7 per 100,000 person-years in a pediatric population¹⁶. Palmer et al. suggested that less than 2% of patients with verified HS experience disease onset before the age of 11 years¹⁷, and Scheinfeld estimated that less than 1% of patients with HS reported disease onset before the age of 18 years¹⁸. However, a recent retrospective cohort study found that approximately 8% of patients with HS reported onset of disease before the age of 13.5 years¹⁵.
Case reports describe pediatric patients with HS as young as 8-9 years of age; these cases were associated with precocious puberty and adrenarche. Another case report describes pre-pubertal onset of severe HS without any signs of puberty or androgen overload.

**HS and obesity**
Retrospective data from outpatient databases suggest a prevalence of 0.17% in children and adolescents (5-17 years) with obesity compared with 0.03% in patients with a normal body weight. Obesity in childhood is furthermore positively correlated with precocious puberty. We aimed to characterize pediatric patients with HS and overweight and obesity including their clinical presentation of HS.

**Materials and Methods**
We characterized cases identified as possibly having HS in a cohort of children and adolescents with overweight and obesity. Overweight was defined as a body mass index (BMI) standard deviation score (SDS) in the range 1.28-2.33 (corresponding to the 90th-99th BMI percentile), and obesity was defined as a BMI SDS > 2.33 according to Danish age- and sex-adjusted BMI charts. The patients were recruited from the cohort of children and adolescents undergoing a multidisciplinary, multifaceted, outpatient childhood obesity treatment program (n=1,572) at The Children’s Obesity Clinic, Department of Paediatrics, Copenhagen University Hospital Holbæk, Denmark, (January 2007 - April 2015). Of the 1,572 patients, 195 randomly selected patients underwent physical examination to screen for HS, acanthosis nigricans, striae distensae, psoriasis, acne, and hirsutism by a pediatrician during their first visit. Patients presenting with skin symptoms indicative of HS were offered a clinical examination by dermatologists (CK & PTR) to verify the HS diagnosis. HS was characterized using the Hurley stage and Sartorius score. Patients provided information on HS symptoms, smoking, and familial disposition to obesity and HS. Information on psychiatric comorbidities was obtained from the electronic patient records. Patients diagnosed with HS were offered treatment at the Department of Dermatology, Zealand University Hospital, Roskilde, Denmark.

A cohort of normal-weight children (n=785) recruited in a previous study under The Danish Childhood Obesity Biobank was used as a reference population to compare with the cohort.
with overweight and obesity. The reference cohort was recruited from September 2010 to February 2014 from schools in the region of Zealand, Denmark. We included data on BMI, psychiatric comorbidities, and smoking (passive and active). Exclusion criteria were 1) being a twin, and 2) having a disease requiring medication.

**Statistics**

Continuous data are reported with median and range, categorical data are reported with a frequency distribution. Medians were compared using Mann-Whitney U tests. Rates were compared using Fischer’s exact test. All statistics were performed in “R” statistical software version 3.2.3. P-values < 0.05 were considered significant.

**Ethics**

The study was conducted in accordance with the Helsinki Declaration. The local research ethics committee was contacted and waived the need for formal approval. The Danish Data Protection Agency (Datatilsynet) registered the study and the data collection. All participants and legal guardians provided informed consent.

**Results**

A total of 195 children and adolescents with overweight and obesity underwent screening for dermatological conditions including HS. Nine patients were screened positive for HS. Six patients were examined for HS by a dermatologist. Five patients demonstrated clinical HS, one patient had severe acne, but not HS. The remaining three patients were unable to participate despite repeated telephone calls and emails.

Four of the five patients with HS had a positive family history of HS from either paternal or maternal side or both. Two of five patients had a sibling with HS. None had onset of disease before puberty. One patient with HS was actively smoking cigarettes. The patients with HS were significantly more exposed to passive smoking than the children in the population-based cohort (4 of 5 vs. 136 of 440, P = 0.036). Four of five patients with obesity and HS had psychiatric comorbidity. Three patients with HS had been diagnosed with autism spectrum disorders, two patients exhibited anxiety, and one patient exhibited attention deficit hyperactivity disorder (ADHD). The rate of psychiatric comorbidity was significantly higher.
in the HS group (n=4/5) than in the cohort without HS (n=7/190) (P < 0.0001), and the population-based cohort (n=2/785) (P < 0.0001) (Table 1).

Clinically, all patients with HS had mild disease with Hurley stage 1, and a median Sartorius score of 9 (range: 3-31) (Table 2). Four patients with HS presented axillary involvement, and one patient presented boils in the buttocks area. All five patients reported more than two boils in the axillae during the past six months, two patients reported inguinal involvement, and three patients reported involvement of both the buttocks and in “other regions.”

Discussion

Overweight and obesity may be pathogenic factors of HS. Children with obesity are at higher risk of being obese in adulthood\(^2^8\); thus this patient group is likely to be exposed to overweight or obesity for a longer period of time than patients developing overweight or obesity during adulthood. Obesity has a negative impact on treatment outcomes for HS\(^2^9^-^3^1\). Consequently, patients with paediatric HS and overweight or obesity might represent a subpopulation of patients with HS with recalcitrant disease.

In the present study, patients diagnosed with HS exhibited Hurley stage 1 with mild symptoms only, while most published reports on children or adolescents describe severe HS\(^3^2\). We suggest that this discrepancy reflects a publication bias rather than prospective population screening.

Tobacco exposure is another suspected predisposing factor for the development of HS\(^4^-^3^3^-^3^5\). Passive smoking is measurable in children’s body fluids\(^3^6\) and is shown to affect skin disease\(^3^7\), and negatively affects the outcome in inflammatory bowel disease\(^3^8^-^3^9\). In this study, patients with HS were significantly more exposed to passive smoking compared with the population-based cohort (P = 0.036). The difference in smoke exposure might, however, have been less pronounced if patients with asthma who required inhalers were included in the population-based cohort. Thus, this difference may be subject to confounding in our study. Future studies should investigate the possible association between smoking and HS further.

Approximately one of three patients with HS reported a positive family history of HS\(^4^-^1^5\). In the present study, four of five patients with paediatric HS had a parent with HS, suggesting a
strong genetic component. The epidemiological study by Decker et al. tied early-onset of HS with severity and inheritance\textsuperscript{15}.

Somewhat surprisingly, four of five patients with HS had psychiatric comorbidity (ADHD, anxiety, or autism). In adults, HS has been associated with depression and anxiety possibly related to the stigmata and pain of HS\textsuperscript{7,40,41}. Childhood obesity is known to be associated with ADHD\textsuperscript{42,43} and autism spectrum disorders\textsuperscript{44}. Hence, the observation may result from psychiatric morbidity in the examined cohort rather than an association with HS. The prevalence of psychiatric comorbidity was, however, significantly higher in the HS group compared with the obese cohort (P < 0.0001, table 1). The significant difference between the population-based cohort and the HS group (P < 0.0001) might be a result of confounding due to the exclusion criteria of diseases requiring medication in the population-based cohort.

**Limitations**

Few studies on HS in children and adolescents have been published, and existing studies may be influenced by publication bias, possibly reporting more severe disease and higher rates of comorbidities than that of the average paediatric patient with HS. We aimed to investigate the clinical features of HS in children and adolescents with overweight and obesity. Our study is limited by our sampling method, convenience sampling, as only 195 of 1,572 patients with overweight and obesity underwent screening for skin disease including HS. In addition, the exclusion of patients with diseases requiring medication from the population-based cohort limits the reliability of the comparisons between the population-based cohort and the other groups. Firstly, there might have been HS patients who were excluded from the population-based cohort due to this exclusion criteria. However, the low prevalence of early-onset HS markedly limits the impact of this possible confounder. Secondly, the prevalence of psychiatric comorbidities may be counterfeit low compared with the background population. Though, this possible confounding cannot explain the significant difference in the prevalence of psychiatric comorbidities in the HS compared with the obese cohort.

**Conclusion**

Nine cases with HS were identified by screening of 195 children and adolescents with overweight and obesity. Of these, six were examined by dermatologist of whom five presented clinical HS. All cases were mild, and most patients had positive family history with
HS and psychiatric comorbidity. To minimize the negative psychosocial impact of HS, increased awareness, screening and treatment for HS may be required in a paediatric population with overweight and obesity.

Acknowledgements
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References

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Tables

Table 1: Characteristics of patients with HS and overweight/obesity, patients with overweight/obesity, and the Danish pediatric reference cohort.

<table>
<thead>
<tr>
<th></th>
<th>1. Patients with HS and obesity (n=5)</th>
<th>2. Patients with overweight/obesity, not HS (n=190)</th>
<th>3. Population-based cohort (n=785)</th>
<th>P (1 vs. 2)</th>
<th>P (1 vs. 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age at entry into the</td>
<td>14.5 (8.4–17.0)</td>
<td>13.7 (8.0–17.9)</td>
<td>12.5 (8.0–18.0)</td>
<td>0.54</td>
<td>0.28</td>
</tr>
<tr>
<td>biobank (range)</td>
<td>Sex, boys/total</td>
<td>Median BMI SDS (range)</td>
<td>Children with psychiatric comorbidity/total</td>
<td>Children actively smoking/total</td>
<td>Children exposed to passive smoking in the home/total</td>
</tr>
<tr>
<td>----------------</td>
<td>-----------------</td>
<td>------------------------</td>
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<td>-------------------------------</td>
<td>----------------------------------------------------</td>
</tr>
<tr>
<td></td>
<td>2/5</td>
<td>3.63 (2.83–4.16)</td>
<td>4/5</td>
<td>1/5</td>
<td>4/5</td>
</tr>
<tr>
<td></td>
<td>89/190</td>
<td>3.01 (1.68–6.17)</td>
<td>7/190</td>
<td>7/179</td>
<td>100/184</td>
</tr>
<tr>
<td></td>
<td>317/785</td>
<td>0.35 (-3.16–3.37)</td>
<td>2/785</td>
<td>11/460</td>
<td>136/440</td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>0.059</td>
<td>&lt;0.0001*</td>
<td>0.201</td>
<td>0.381</td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>&lt;0.0001*</td>
<td>&lt;0.0001*</td>
<td>0.123</td>
<td>0.036*</td>
</tr>
</tbody>
</table>

HS = Hidradenitis Suppurativa. BMI = Body mass index, SDS = standard deviation score.
* = Significant difference

**Table 2:** Characteristics of pediatric patients with HS (n=5)

<table>
<thead>
<tr>
<th></th>
<th>Median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at debut (years)</td>
<td>15 (14-17)</td>
</tr>
<tr>
<td>Hurley stage</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Sartorius score</td>
<td>9 (3-31)</td>
</tr>
<tr>
<td>Skin trouble VAS</td>
<td>5 (1-5)</td>
</tr>
<tr>
<td>Flares per year</td>
<td>12 (3-96)</td>
</tr>
</tbody>
</table>

VAS = Visual analogue score