

Outcomes of Children Presenting with Signs of Early Puberty to a Tertiary Pediatric Endocrinology Service

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Aims:

The aim of this study is to review the outcomes for children who present with early puberty symptoms to a tertiary paediatric endocrinology clinic. There are two main aims: -

- 1) Documenting the number of children who were considered to have a variation of puberty (eg. premature adrenarche, thelarche) or a pathological diagnosis (eg. central precocious puberty, congenital adrenal hyperplasia (CAH) or a gonadal tumour).
- 2) Review the initial and subsequent investigations to assess if there is scope to focus or rationalise the investigations in conjunction with initial clinical findings.

Background to the project:

Precocious puberty (PP) * is typically defined as the beginning of the development of secondary sexual characteristics (as the first step towards achieving reproductive potential) in boys and girls before the ages of 8 and 9, respectively. [Mul D, Pubertal development in The Netherlands 1965 - 1997 2001; 50: 479–86.]. PP is a range of condition that can sometimes present as isolated premature thelarche, adrenarche, or menarche in addition to the progressive development of all secondary sexual traits.

A crucial factor in the substantial long - term biological, psychological, and physiological repercussions of PP is effective diagnosis and management of the condition. Untreated PP and early onset of puberty have been linked to reduced adult height, an increased risk of developing metabolic syndrome, dyslipidemia, dysglycemia, cardiovascular problems, hyperandrogenism, a higher risk of developing breast cancer, increased psychological disturbance, increased risk - taking behavior, and increased sexual activity. [Willemsen RH, Et Al. Pros and cons of GnRHa treatment for early puberty in girls. *Nat Rev Endocrinol.*2014; 10: 352–63.] The diagnosis and treatment of PP are, however, made difficult by the lack of standardized age cut - offs for clinical diagnosis, the variety of clinical presentations, the wide range of pharmacologic treatments available, and the absence of standardized biochemical parameters for tracking therapeutic response and evaluating long - term outcomes.

Therefore, the purpose of this proposal is to examine the relationship between the presenting symptoms of patients

with PP to tertiary endocrine clinics, the findings of their additional investigations, and their ultimate diagnosis.

Keywords:

Premature thelarche: Premature breast enlargement

Adrenarche: production of androgens that makes the body produce pubic hair and body odour.

Menarche: production of menstruation

Objectives/research questions:

- To estimate the number of children who were eventually diagnosed with premature adrenarche, central precocious puberty, congenital adrenal hyperplasia or other and method of diagnosis.
- Frequency of abnormalities identified on MRI* scans in those with CPP*.
- Incidence of CAH* in those with features of premature adrenarche.
- Change in height SDS* between first and subsequent appointment and whether it predicted an underlying pathology.

Details of the project:

Type of the study: Retrospective Cohort Observational Analytic study

Subjects are:

Males aged 0 to 9 years and females aged between 0 to 8 years old presenting to a single tertiary center (Bradford Teaching Hospitals),

With signs of PP, such as:

- Breast growth and first period in girls.
- Enlarged testicles and penis, facial hair and deepening voice in boys.
- Pubic or underarm hair.
- Rapid growth.
- Acne.
- Adult body odor.

Between the period January 2011 to January 2021 - 10 - year data collection.

*Identifying the sample, using the:

- PPM+* (Patient Pathway Manager) is LTHT's* electronic health record, built on the latest web technology and benefiting from a program of continuous development to deliver an agile, multi - functional EHR*.

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- LGI* Archive: the collection includes, but is not limited to, Board of Management minutes from 1767 onward, hence help in gathering information before 2021: can be used for previous details about patients if needed

The electronic letters from Bradford are stored on the LGI drives and on ppm

Consent: I would apply for export permissions to PPM files as well as permission to access the Hospital's system in general, to enable me access files in my own office at home.

Statistical method:

For the analysis of retrospective study data, I would apply Pearson's correlation coefficient (r) & chi - square tests for the statistical significance of the observed correlation between the proportion of patients with varied final diagnosis of PP and their presenting signs, investigation abnormality results.

Questionnaires:

Not used

Feasibility:

Time scale:

- June 2023: scheduled to meet with my clinical supervisor who is a pediatric endocrinologist consultant in LGI, for in - depth discussion.
- July 2023: Make a list of patients seen with PP. Create a template for data collection
- Aug to Dec 2023: Data collection includes the patient's age, gender, height, pubertal signs, and details when they first visited an endocrine clinic, as well as serial blood and radiological tests, their findings, and the patient's height when they subsequently visited. Additionally, each person's concluding diagnosis.
- January till February 2024: statistical analysis and conclusions
- March - May 2024: finalizing the study
- June: Submitting the research

Funding

This is a retrospective observational study where required patient data can be obtained from the hospital's PPM system and previous patients' records (LGI Archives before 2021) I would not expect any costs to be incurred in getting access and using existing patient records.

Some obstacles that I can potentially face:

A barrier can be that certain data are missed throughout the data collection procedure. Given the use of out - of - date web systems from 2020, which are thankfully not heavily employed in this study. They have only recently been upgraded to prevent form submission before filling out some necessary information, something that could be fairly beneficial to verify some data are unquestionably there. Unblinded data collection: Due to the study's retrospective character, this is an issue.

It is possible that the aims may have to be modified depending on the number of patients

Ethical approval/sources of funding:

Retrospective data gathering from the PPM systems over a predetermined period is required for this project. These tests would have been administered to the patients as part of ongoing clinical care. As a result, they won't be subjected to any additional hazards or time demands because I won't be interacting with them. When the children attended their endocrine appointment in Bradford for diagnosis and management, their parents merely consented as part of clinic attendance. In order to conduct an audit or service evaluation of the department's operations and provide recommendations for improvement, I will be accessing their records. As a result, since audit is a requirement of NHS clinical governance, I would not require explicit agreement from each patient.

All data will be gathered by me, and it will be managed in a private way with password - protected software and the prompt deletion of Excel folders after use. In order to continue having access to patient data when I leave the department in September 2023, I will also ask the IT team for extended access.

References

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Index:

CAH: Congenital Adrenal Hyperplasia
 CPP: Central Precocious Puberty
 EHR: Electronic Health Record
 LGI: Leeds General Infirmary
 LTHT: Leeds Teaching Hospitals NHS Trust
 MRI: Magnetic Resonance Imaging
 PP: Precocious Puberty
 PPM: Patient Pathway Manager
 SDS: standard deviation score