

Topical Estrogen Treatment in Paediatric Labial Adhesions

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ABSTRACT

Objective: In compliance with the previous literature, this study was carried out to assess the magnitude of the disorder of labial adhesions in paediatric population presenting at our MCH centre and to observe the success of topical estrogen therapy in these cases that might lead to avoidance of surgical intervention.

Design: Prospective case control study.

Place & duration of study: MCH Centre of CH & ICH Lahore from January 2008 to December 2008.

Patients and methods: This study comprised of 150 girls belonging to paediatric age group (8 months to 05 years). Detailed history, general physical as well as gynecological examination followed by relevant investigations were undertaken. Topical Premarin therapy with petroleum jelly and care of vulvar hygiene were strictly advised to all mothers until resolution of symptoms. Follow up sessions were planned to observe the compliance as well as for monitoring the phasic response to treatment and for surveillance of any complications or recurrence.

Results: Our observations revealed that of 150 cases in our study with mean age being 3.4 years, 90% patients were demonstrating >50% adhesions of labia with partial to complete obscuring of the vaginal orifice. After premarin treatment, complete cure was achieved within a mean duration of 6.14 weeks (range 3-10 weeks). Post treatment follow up findings were the resolution of all notified mild complications in a brief period of mean 4.5 weeks with recurrence observed in only 2% cases that stood apart in another 2-3 months.

Conclusion: Labial adhesions is a common and clinically quiescent disorder and calls for opting conservative medical management with premarin or similar drugs, without exposing them to potential dangers of surgery.

Key words: Labial adhesions, Topical Premarin therapy, Vulvar hygiene

INTRODUCTION

Labial adhesions is an acquired condition in which the folds of skin just outside the vagina (labia) stick together in the midline causing partial or complete occlusion of the vaginal opening¹. Other names for this condition are vulvae fusion, atresia of the vulva, synechia of the vulva, occlusion of the vestibule, atresia vulvae superficialis, adhesion of the labia minora, and agglutination of the labia minora². This condition should be distinguished from congenital deformities³, as it often gives the appearance that the opening of the vagina has closed off⁴, but visually there is a midline raphe (line of fusion) present with labial adhesion that would not be apparent in a congenital condition³. It is secondary to vaginal inflammation or irritation due to any cause⁵; mostly exposure to irritants like fabric softener residue, perfumed soaps, or bits of stool; or a prolonged exposure to damp (as in wet diapers) are the culprits⁴. Once the superficial epithelium of the labia

is denuded, subsequent healing leads to fibrous adhesions between the labia⁶, this being supplemented by HYPOESTROGENISM at extremes of ages; prepuberty or post menopausal⁷. Labial fusion is most commonly noted between 3 months⁸ (just after the estrogen a baby received at birth from mother has tapered off)⁹ and 4 years of age and has a peak incidence of 3.3% between 13 months and 23 months of age⁸. The relative incidence in the US is 1-2% of females aged 3 months to 6 years. Incidence of labial adhesions worldwide is unknown but presumably similar to US incidence¹⁰. Labial adhesions are generally asymptomatic and not a common cause of urologic or gynecologic morbidity but may predispose to asymptomatic bacteriuria and urinary tract infection¹¹ or rarely urinary outflow obstruction resulting in bladder distention or hydronephrosis¹². Since labial fusion rarely persists beyond puberty, some investigators do not recommend treatment whereas others do so^{13,14,15}. Currently vulvar hygiene measures combined with topical estrogen is the best preferred treatment¹⁶ which may be followed by gentle manual separation but traumatic lysis should be avoided¹⁷. Depending upon the maturity of the child and the expectations of the parents, surgical separation can be performed if

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medical care does not result in a favorable outcome but should be restricted for resistant cases or very thick adhesions¹⁸. Previous literature reveals that treatment of persistent or recurrent labial agglutination with topical estrogen therapy following detailed application instruction leads to avoidance of surgical intervention in at least 35% of cases¹⁹. Premarin is the commercial name for compound drug consisting primarily of low dose conjugated estrogen (0.625 mg) isolated from pregnant mare's urine²⁰. The major forms of estrogen in Premarin are estrone (>50%), equilin (15-25%) and equilinenin²¹. The estrogens in Premarin are often called "conjugated equine estrogens" (CEE) with hydrophilic side-groups attached such as sulfate. Thus, estrone sulfate is actually the major molecule in Premarin which is converted to estradiol²⁰. There is no clear consensus for the duration of treatment with topical estrogen²². Using topical estrogen cream may induce other transient estrogen effects in the patients, including breast enlargement, vulvar or nipples pigmentation. These effects resolve usually after cessation of therapy which may sometimes cause a brief 'mini-period' or vaginal break through bleeding which is self-limited and not a cause for concern²³. Recurrence is however reported to be common¹⁷.

In compliance with the previous literature, this study is carried out to observe the magnitude of the disorder in paediatric girls presenting to our Maternal and Child Health (MCH) Centre and to assess the success of topical premarin treatment in such cases.

MATERIALS AND METHODS

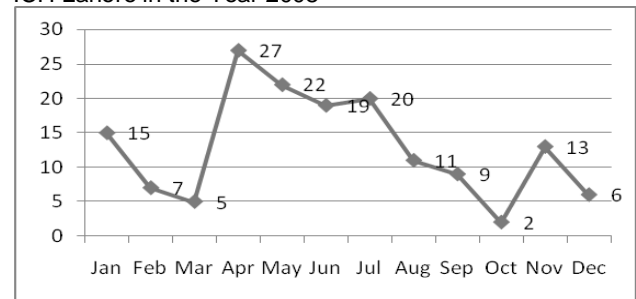
This prospective observational study comprised of 150 girls selected through randomized non probability sampling, belonging to paediatric age group (8 months to 05 years), reported at the MCH Centre of Children Hospital and Institute of Child Health (CH & ICH) Lahore from January 2008 to December 2008, after taking informed written consent from the parents. The patients were included after detailed vulvar examination. Exclusion of the cases, with congenital or acquired ambiguous genitalia, or those who had been treated in the past for this condition, was carried out. Detailed history, general physical as well as gynecological examination followed by relevant investigations including complete urine examination, urine culture (where required) and abdomino-pelvic ultrasonography (A/P USG) were undertaken. Topical Premarin therapy with petroleum jelly and care of vulvar hygiene were strictly advised to all mothers upto resolution of symptoms. Weekly follow up sessions were planned to observe the compliance as well as for monitoring the phasic response to treatment. Parents were also advised to

carry out a monthly post treatment follow up for at least 3-4 months for surveillance of any complications or recurrence.

RESULTS

After a comprehensive review of the paediatric gynaecological disorders reported at the MCH centre of CH & ICH in the year 2008, we were able to segregate a total of 160 cases of labial adhesions presenting to the department with variable frequency in each month (Graph:1), the peak being in the hot and humid climatic era.

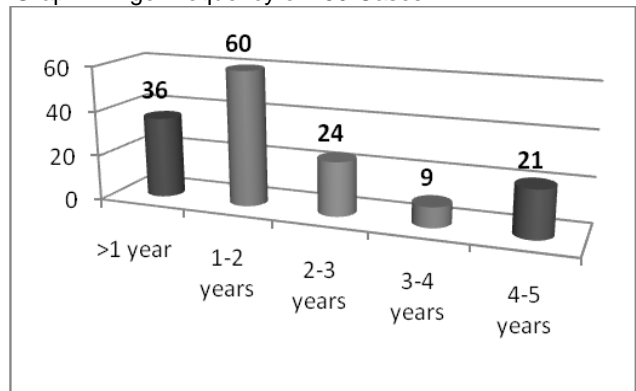
Graph 1: Cases of Fused Labia at MCH Centre of CH & ICH Lahore in the Year 2008



Graph 1 shows the cases of fused labia at MCH Centre of CH & ICH Lahore in the year 2008. Note the peak lies between the months of April-July.

Within these 160 cases, we included a total of 150 patients in this study, who met inclusion criterion. These cases presented with variable age frequencies (Graph 2) and were grouped in yearly batches from less than 1 year to 05 years of age at maximum.

Graph 2: Age Frequency of 150 Cases



Graph 2 shows age frequency of 150 cases included in the study. Most of the girls, 40% (n=60), reported between the age group of 1-2 years.

Detailed clinical history (Table 1) depicted dysuria being the most frequent presentation in 50%(n=75) cases.

Table 1: Clinical features of 150 cases

Asympt	Dysuria	Dribbling/spraying of urine	Others
54	75	21	17

Table 1 portrays the clinical features of 150 cases of which 11.3% (n=17) presented with miscellaneous systemic or congenital disorders like recurrent diarrhea or urinary tract infection, congenital heart diseases, insulin dependent diabetes mellitus etc.

Vulvar examination findings revealed that 90% (n=135) and only 10% (n=15) patients presented with >50 % (Fig:1) and <50% adhesions of the labia (Fig:2) with partial to complete obscuring of the vaginal orifice.

Fig:1- Complete occlusion of the vaginal orifice, below the clitoris, due to severe labial fusions. Note the midline raphe characteristic of an acquired origin of this disorder.



Fig:2- This figure shows partial occlusion of the vaginal orifice, below the clitoris, with a minuscule opening in the middle of otherwise fused labia.

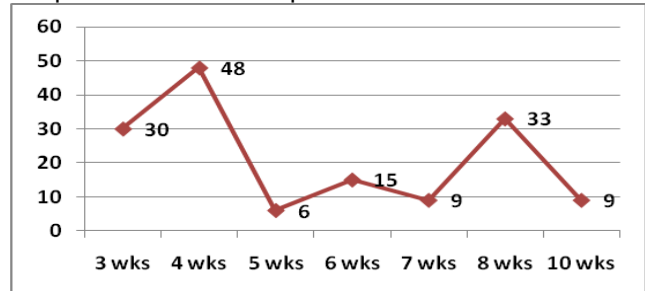


Investigative findings out in the open were unremarkable A/P USG in 100% (n=150) cases while 20% (n=30) presented with urinary tract infection and 40% (n=12) of these had positive urine culture for

bacterial growth mainly *E.coli*, *Pseudomonas aeruginosa*, *Trichomonas vaginalis* etc.

After topical premarin treatment, complete cure with successful parting of the labia was achieved within 3-10 weeks in all cases (Graph:3).

Graph3: Treatment Responses In 150 Cases



Graph 3 shows the treatment responses in 150 cases. The maximum 32% (n=48) patients recovered with complete resolution of symptoms in 4 weeks. Though variable, but the response was quite satisfactory (Fig:3, 4) to the patients, their parents as well as for the physician.

Fig:3- Complete separation of labia minora (red arrow) after 4 weeks of premarin treatment in the same patient



Note the pigmentation of the vulva (blue arrow) as compared to Fig:1.

Avoidance of recurrence was achieved by emphasis on the importance of meticulous introital hygiene to minimize inflammation and application of a petroleum ointment for at least 1 month after separation.

During follow-up, however, mild premarin application related complications (Graph:4) were notified with most of the girls, 20% (n=30), presenting with mild to severe vulvar pigmentation (Fig:5), that in turn was resolved after 4-5 weeks of cessation of therapy. Local redness and slight breast enlargement was receded in 4 weeks after therapy. Post treatment follow up of only 2% (n=3) patient illustrated recurrence of the disease 6 weeks after the cessation

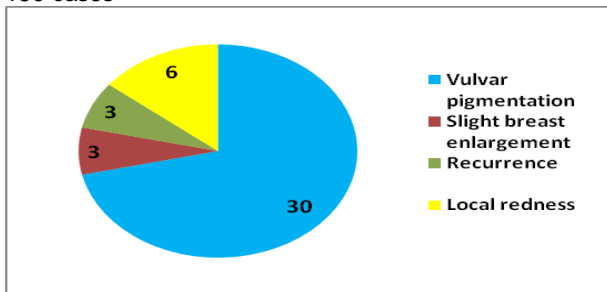
of therapy which ultimately improved within 3-4 weeks of resuming premarin treatment.

Fig:4- Complete separation of labia minora (red arrow) after 6 weeks of premarin treatment in the same patient as in Fig:2.



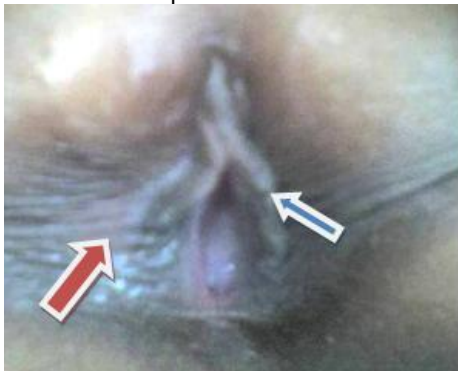
Note the vulvar skin (blue arrow) devoid of pigmentation due to precise application of premarin.

Graph 4: Topical Premarin therapy related complications in 150 cases



Graph 4 shows the complications related to topical premarin therapy in 150 cases. Vulvar pigmentation was noted at most in 20% (n=30) whereas only 2% (n=03) showed recurrence.

Fig:5: Severe pigmentation of the vulva (red arrow) and the separated labia minora (blue arrow) after 8 weeks of premarin treatment in a patient.



Applying Chi-square test, no significant correlation was found between age of the 150 cases and premarin application related complications ($p=2.19$) or duration of treatment ($p=0.12$).

DISCUSSION

Our findings of this study demonstrated that labial adhesions is a common paediatric gynaecological disorder (Graph:1) with mean age of presentation being 3.4 years (range 8 months-5 years) in our part of the world. According to José L, labial adhesions was reported in 17.6 percent of all gynecological pathologies at Valencia clinic from April 2005 to April 2006 with the age range of these 20 girls being from 2 months to 28 months. The mean age of 4.66 ± 1.72 months and 4 years was reported by Jose and Girton respectively^{5,26}.

Labial adhesions in prepubertal girls were successfully treated with topical estrogen without the need for surgery in a series of 36 patients at a single center by Jane E Dopkin in the year 2003 of which a total of 22% had symptoms, including dysuria, vulvar itching, odor, and discharge²⁷. The patients in our study revealed dysuria mostly 50% followed by dribbling or spraying of urine in 14% cases.

The mean duration of estrogen treatment was 2.4 months (range, 1 to 3.5 months) by Opipari²⁸. In those successfully treated by Khanam et al, the duration of treatment was 1 week in 8 (36%) patients, 2 weeks in 10 (45%) patients, 3 weeks in 3 (14%) patients, and 4 weeks in 1 (5%) patient²⁹. Capraro and Greenberg treated 50 patients with labial fusion with a topical estrogen cream. Of 47 patients with adequate follow-up, 42 (89%) had good results after 2 to 4 weeks of therapy³⁰. Aribarg treated 25 girls with severe adhesion of the labia minora. Topical estrogen therapy was successful within a month in 22 (88%) patients whereas the duration of treatment varied from 1 to 8 weeks³¹. Jane Dopkin and her associates, in a series of 36 patients, demonstrated the average time to resolution of the adhesions being 2.6 weeks, with a range of 0-9 weeks. Patients who began with less than 50% adhesion required no more than 4 weeks of estrogen treatment. Girls with more than 50% adhesion occasionally required more than 6 weeks of treatment before manual separation was possible²⁷.

Five patients developed vulvar pigmentation, which lasted for a mean of 1.5 months. One patient developed breast enlargement, which lasted for 1 month by Opipari²⁸. 18 Of the 25 patients treated by Aribarg slight vulval pigmentation occurred in all patients, but the pigmentation disappeared after the medication was discontinued³¹. Of the 50 patients treated for 2 to 4 weeks with topical estrogen therapy

by Capraro and Greenberg, 3 developed vulval pigmentation, 3 complained of breast tenderness, and 1 manifested both adverse events. The adverse events disappeared after topical estrogen therapy was discontinued³⁰. According to Bacon, four patients had vulval erythema and pain, and 2 had breast "budding." These adverse events disappeared after the topical estrogen therapy was discontinued. Increased body hair was noted in 1 of the 2 patients who developed breast "budding." The body hair partially resolved after the topical estrogen therapy was discontinued²³. None of our patients developed increased body hair or any of those reported in the literature developed vaginal bleeding during or subsequent to topical estrogen therapy. The adverse events from topical estrogen therapy are usually mild and resolve with the cessation of the treatment. In compliance with these authors, in our experience too, the use of topical estrogen cream is safe for the treatment of labial fusion.

Murann performed a retrospective chart review of 259 girls with symptomatic labial fusion referred to a Pediatric and Adolescent Gynecology Clinic. The girls were treated with topical estrogen therapy for 10 to 14 days. The fused labia resolved in only 121 (47%) patients. One hundred and thirty-eight girls who did not respond to topical therapy had their labial adhesions separated in the office under topical anesthesia. The procedure was successful in 112 patients. The remaining 26 patients required surgical separation of the labia minora under general anesthesia. This study by Muram reported an especially low success rate with topical estrogen therapy³².

In a mean duration of follow-up of 3.1 months, no recurrence of labial fusion was observed during by Opipari²⁸. Six of 36 patients were known to have a recurrence of the adhesions by Dopkin²⁷. In the retrospective study by Muram recurrence developed in 14 (11.6%) of 121 patients treated with topical estrogen cream³².

In our study, the success rate was 98% after a mean duration of estrogen treatment of 3.5 weeks. In a mean follow-up of 2.4 months, recurrence was observed only in 2% (n=6) girls and that too was treated by resuming the treatment for another 2 months. We (in compliance with ref:16 &17) do not recommend or resort to mechanical separation of the labia minora, which can be physically and emotionally traumatic. Parents satisfaction was the foremost outcome because comparable to the surgical treatment, the patients as well as their parents were being spared of the agony, pain, procedural complications, the cost and the hospital stay.

CONCLUSION

As pediatricians, we are tied up to allow children the benefits of conservative medical management without exposing them to potential dangers of surgery. Labial adhesions is clinically and prognostically a disorder with minimal harm to the patient and calls for opting a medical cure with premarin or similar drugs, resultantly achieving a success as a treatment modality of choice for the paediatric gynaecologists.

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REFERENCES

- Balwin DD: Common Problems in Pediatric Gynecology. *Urol Clin North Am.* 1995; 22: 161-76.
- Clair DL, Caldamone AA. Pediatric office procedures. *Urol Clin North Am.* 1988;15:715-23.
- Elder JS: Congenital Anomalies of the Genitalia. 6th ed. In: Campbell's Urology. 1992; 1920-38
- Labial Adhesions by Marjorie Greenfield. Available online at <http://www.drspock.com/article/0,1510,5892,00.html>
- Stephanie Girton, Colleen M. Kennedy, Rudolph P. Galask: Characteristics and outcomes of 16 patients with symptomatic labial adhesion. *The Internet Journal of Gynecology and Obstetrics* 2007;7: 1
- Starr NB. Labial adhesions in childhood. *J Pediatric Health Care* 1996;10:26-7.
- Herieka E, Dhar J. Labial adhesions following severe primary genital herpes. *Sex Transm Infect* 2001;77:75
- Kumar RK, Sonika A Charu, Neena M, Sunesh K. Labial adhesion in post-pubertal girls : case report. *Sabinet* 2005;15:22-23
- Leung AK, Robson WLM, Tay-Uyboco J. The incidence of labial fusion in children. *J Pediatr Child Health.* 1993; 29:235-6
- Labial adhesions. Available online at http://www.babycenter.com/0_labial-adhesion_10889.bc.
- Kenneth G Nepple, Madhu Alagiri, Christopher S Cooper. e-Medicine - Labial Adhesions. Available online at <http://emedicine.medscape.com/article/953412-overview>.
- Leung AK, Robson WLM. Labial fusion and asymptomatic bacteriuria. *Eur J Pediatr* 1993;152:250-251.

13. Leung AK, Robson WLM. Labial fusion and urinary tract infection. *Child Nephrol Urol* 1992; 12:62-4.
14. Wheeler RA, Buttge DM. Urinary obstruction due to labial fusion. *Br J Urol* 1991;67:102
15. Soyer T. Topical estrogen therapy in labial adhesions in children: therapeutic or prophylactic? *J Pediatr Adolesc Gynecol* 2007;20:241-4.
16. Schroeder B. Pro-conservative management for asymptomatic labial adhesions in the prepubertal child. *J Pediatr Adolesc Gynecol* 2000;13:184-5.
17. Leung AK, Robson WL, Kao CP. Treatment of labial fusion with topical estrogen therapy. *Clin Pediatr* 2005; 44: 245-7.
18. Muram D. Treatment of prepubertal girls with labial adhesions. *J Pediatr Adolesc Gynecol* 1999;12:67-70
19. Nurzia MJ, Eickhorst KM, Ankem MK, Barone JG: The surgical treatment of labial adhesions in pre-pubertal girls. *J Pediatr Adolesc Gynecol* 2003;16:21-3.
20. Kumetz LM, Quint EH, Fisseha S, Smith YR. Estrogen treatment success in recurrent and persistent labial agglutination. *J Pediatr Adolesc Gynecol*. 2006;19:381-4.
21. Premarin. Available online at <http://premarin.org/>.
22. PREMARIN® Vaginal Cream. Product Monograph. Available online at [Premarin\Premarin_VC_PM_.PDF](#)
23. Bacon JL. Prepubertal labial adhesions: evaluation of a referral population. *Am J Obstet Gynecol* 2002;187:327-32.
24. Premarin side effects. Available online at www.drugs.com/sfx/premarin-side-effects.html - 37k.
25. T. Nebesio, E. Eugster. Current concepts in normal and abnormal puberty. *Current Problems in Pediatric and Adolescent Health Care* 2005;37:50-72.
26. José L; Elsa L; David M; Carlota M; Nieves P. Labial adhesions: management in a gynecological pediatric clinic at Hospital Metropolitano del Norte in Valencia Venezuela. *Salus* 2008;12:8-11.
27. Jane E. Dopkin. Labial adhesions in prepubertal girls: OB.GYN. NEWS. Available online at http://findarticles.com/p/articles/mi_m0CYD/is_17_38/a_i_107895633
28. Opiari AW Jr. Management quandary. Labial agglutination in a teenager. *J Pediatr Adolesc Gynecol* 2003;16:61-2.
29. Khanam W, Chogtu L, Mir Z, Shawl F. Adhesion of the labia minora-a study of 75 cases. *Aust N Z J Obstet Gynaecol* 1977;17:176-7.
30. Capraro VJ, Greenberg H. Adhesions of the labia minora: a study of 50 patients. *Obstet Gynecol* 1972;39:65-9.
31. Aribarg A. Topical oestrogen therapy for labial adhesions in children. *Br J Obstet Gynecol* 1975;82:424-5.
32. Muram D. Manual separation of labial adhesions in prepubertal girls. *J Pediatr Adolesc Gynecol* 2000;13:183-4.