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## Review Article

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## An approach to women with Labial agglutination at different stages of life - A Review

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### Abstract

#### Keywords

Labial agglutination;  
vulvar fusion;  
Topical estrogen;  
imperforate hymen;  
urinary  
pseudoincontinence

**Introduction:** Labial agglutination (LA) or vulvar agglutination is seen in females of different age groups. Careful and systematic genital examination is key to correct diagnosis and to differentiate it from other conditions. Causes and management at different age groups differ substantially. **Materials and Methods:** A review of all published data related to management of labial agglutination was conducted. The online databases SCIENCE DIRECT, PUBMED, CINHALL, EBSCO, SCOPUS, and UPTODATE were used for identifying relevant studies. Medical subject handling terms (MeSH) and free text terms such as labial agglutination and vulvar agglutination were used in combination with children, reproductive age and postmenopausal women for the search of all published articles regarding the presentation, causes and management. The data was compiled and analyzed by systematic review to formulate ideal management approaches relevant to the different age groups. **Conclusion:** LA occurs primarily due to estrogen deficiency in children and elderly though inflammation plays a significant role. It is due to severe inflammation or trauma in adults. Most cases are asymptomatic in childhood. Most common symptoms are urinary in all age groups. Topical estrogen is most effective as first line therapy in children. Reproductive age women need surgical separation in almost all cases. In most menopausal women, manual separation is an effective method of treatment. Topical estrogen is effective for prevention of recurrence. Various modifications of surgical technique can also successfully prevent recurrences.

## 1. Introduction

Labial agglutination constitutes a group of benign conditions which are associated with adhesion of both lips of labia. This can be of various types with milder forms constituting of partial fusion of labia minora to most severe forms being complete fusion of labia minora & majora obliterating urethral meatus. This condition is often also loosely referred to as vulvar agglutination, fused labia and vulvar fusion.

### 1.1. Incidence and Prevalence

Incidence of Labial Agglutination (LA) varies in different age groups and worldwide incidence is not available. It is commonest in prepubertal girls, fairly common in menopausal women and rarely seen in reproductive age women. In different studies the reported incidence ranges from as little as 0.6% to as high as 38.9%. [1,2,3,4,5] Reported incidence in the United states was 5% among pediatric population in one study [3] while in another study from UK, cases with labial agglutination consisted of 14% of all referrals to tertiary center in girls. [6] However, as most cases in children are not

reported due to lack of symptoms, the actual prevalence is likely to be higher than reported. [7]

The most frequent age group affected are children between 13 to 23 months in one study and between two to six years in another study. [3, 8]

### 1.2. Materials and Methods

A review of all published data related to management of labial agglutination was conducted. The online databases SCIENCE DIRECT, PUBMED, CINHALL, EBSCO, SCOPUS, and UPTODATE were used for identifying relevant studies. Medical subject handling terms (MeSH) and free text terms such as labial agglutination, vulvar agglutination were used in combination with children, reproductive age and postmenopausal women for the search of all published articles regarding the presentation, causes and management. The data was compiled and analyzed by systematic review to formulate ideal management approaches relevant to the different age groups.

### 1.3. Diagnosis

Diagnosis of LA can be clinical made by careful inspection. Starting from Labia majora, the structures are carefully inspected to identify both labia minora and vaginal opening. In presence of LA there will be fusion of lips of labia minora with or without involvement of labia majora either partially or completely. The typical appearance is a flat appearing genitalia with loss of elasticity and a midline vertical translucent membrane. This membrane may be thin and fragile or may be even dense and thick. When labia

minora is fused with labia majora, labia minora may be non-identifiable or very small. Clitoris may also be non-evident in case of anterior fusion due to presence of scar tissues around. For an accurate diagnosis this condition has to be differentiated from vaginal atresia, Gartner's duct cyst, ambiguous genitalia and imperforate hymen especially in children, [9] where as other mass occupying conditions like skin tags, polyp, urethrocele, prolapse or diverticulum of urethra needs consideration in older females. [Figures-1,2,3,4][10,11,12,13]



Figure-1: Normal vulva in newborn [10]



Figure-3: Ambiguous genitalia [12]



Figure-2: Labial agglutination [11]



Figure-4: Imperforate Hymen [13]

### 1.4. Clinical presentation

There are a wide range of symptoms associated with LA. Most common symptoms are urinary e.g. difficulty in voiding and recurrent urinary tract infection (UTI) although patients can present with vulvar symptoms like burning, itching, pain, dyspareunia, discomfort during menstruation, vaginal discharge and even pseudocyst formation. [14,15,16]

Though LA cannot cause UTIs per se, it is reasonable to think that the pooled urine (which is) retained above the fusion line, can facilitate ascending infection. This has also been demonstrated by modalities like voiding urethrocytography in these females. [17]

Most of the cases in children are asymptomatic and are missed easily. When present, symptoms are likely to be dribbling from the pooled urine, of vulvovaginitis or of UTI. [9,18,19,20]

### 1.5. Causes

As LA is common before puberty and after menopause, it is thought that estrogen deficiency plays a major role in formation of adhesion. [1,2] Though believed to be a congenital condition, it is very rare to see fused labia in newborn infants. [1,3,21] This can be explained by protective effect obtained from circulating maternal estrogen. In girls before puberty, vulvar injury or inflammation in an estrogen deficient labial epithelium causes scar formation which acts as an adhesion band and causes labial fusion. [22] Vulvovaginitis and even pinworm infestation can be causative factor in adhesion formation in children. [23] Though hypoestrogenism is blamed for LA, when serum estradiol levels were compared among those with or without LA in a study, it was found that there was no statistical difference. [24]

It can therefore be interpreted that both (rather than either one) of these factors should be present for the development of LA. Though they might not be related, in children with adhesions in presence of genital trauma, genital mutilation and sexual abuse should also be suspected. [25,26, 27]

Vulvar skin conditions like lichen sclerosus, lichen planus, pemphigoid, Behcet syndrome, Stevens-Johnson syndrome / toxic epidermal necrolysis and vulvar cancer can present with symptoms similar to LA but these conditions usually have other symptoms pertaining to primary disease in addition.

In women of reproductive age group estrogen deficiency is unlikely, and genital trauma and infections are responsible for majority of the fusions though it can occur spontaneously in some cases. In literature, cases have also been reported following spontaneous or vacuum assisted delivery,[28-37] as a complications of surgery like pelvic floor repair, [35-37] infections especially after Herpes simplex I and II infection [38,39] and pemphigoid.[40] LA has also been associated with lichen sclerosus, in which adhesions are characteristically dense and difficult to treat. These adhesions when seen in children, can persist into puberty and adulthood. [41]

## **2. Management of agglutination at different age groups**

### **2.1. Management of labial agglutination in prepubertal girls**

There is much debate on whether treatment is required in all cases of LA. Only one study involving ten girls have concluded a 100% spontaneous resolution when followed up till 18 months of age.[42] [Table-1] As most of the cases of LA in pediatric age group are asymptomatic, and it rarely persists after puberty (evident by limited case reports), [42,43] it is rational to have conservative management in patients without symptoms. Counseling parents about the prognosis and possibility of spontaneous resolution in cases with small adhesions helps in prevention of unnecessary interventions and is preferred by some physicians. [44,45] Regular screening for bacteriuria is advisable in cases where wait and watch management is undertaken as in a study by Leung et al it was seen that 6 out of 33 (18%) girls have asymptomatic bacteriuria as compared to 0% in controls with no labial fusion.[3]

In cases where there are symptoms, the adhesion is severe at presentation and parental concern and anxiety is considerable, treatment should be initiated. Topical estrogen application is simple to practice and should be used as first line of management. In the literature, various estrogen preparations has been used for treatment, but conjugated

estrogen seems to be most useful among them. Though there are differences in frequency of applications and duration of treatment most of them used once or twice application for two to six weeks.

Success of topical estrogen treatment is generally high with reported rates of 90%, [1,46] in some studies where as 47 % in another larger study. [7] As the latter study considered failure assessed after only two weeks of treatment, the actual rate might have been high if treatment would have been continued for longer period. Some of the practitioners also recommend daily application of a bland ointment after bath to prevent recurrence of adhesion after estrogen treatment.

Topical betamethasone alone or in combination with estrogen has been used by some of the researchers with a reported success rate of 68% in betamethasone alone in one study [47] while another study reported no significant difference in success rates in groups treated with either agents or the combination [15.4%;15.6%].[48]

One of the studies compared the duration of treatment required and reported that shorter duration of treatment is required in patients using betamethasone as compared to estrogen [1.3 months Vs 2.2 months].[18]

Manual separation of labia is employed in cases with thin adhesion bands which do not respond to topical medication. A mechanical probe like sound, catheter or even swab with cotton tip is used to reach an area behind the fusion line. Traction is then applied pulling it forward to separate the fusion. While topical anesthetics can be used in office settings for the procedure to avoid complications related to systemic anesthesia, it can pose technical difficulties, can be painful to the patients and cause significant discomfort to the parents. [49] In some cultures it may not be socially acceptable as well. For these reasons, local anaesthesia is generally not preferred [1] despite reports of high success rates. [7]

Thick adhesion bands need to be dissected by sharp dissection. Better visualization as well as avoidance of pain and movement can be achieved by surgical separation in operating room under general anesthesia. Various methods have been employed by practitioners to prevent recurrence after separation starting from modifications of standard operating technique [50,51] to use of estrogen post operatively.

In reported studies, various options were used for management including estrogen, betamethasone, manual separation, surgical management and different combinations of them. [52-57] [Table-1]

Table-1: Management of labial agglutination in Pre-pubertal females

Author (Year of publication)	Type of study	No. of cases, age group	Treatment	Comments
Muram D (1999)	Retrospective review	289 cases;	Topical estrogen	Separation in nearly half of patients by topical estrogen. Other half required separation under anesthesia
Jurayyan NAMA (2012)	Case report	5 cases; 6 months to 4 years	Topical estrogen	4 out of 5 responded to topical estrogen. 1 needed surgical separation
Girton S. et al (2006)	Retrospective review	16 cases; 9 months to 34 years	Topical estrogen cream; once a day for 1 week and 3 times a week for 4-6 weeks	9 experienced complete resolution 6 needed surgical separation under anaesthesia
Mayoglou L et al (2009)	Retrospective chart review	151 cases; 0.25 to 8.75 years	Topical estrogen Topical betamethasone	Patients treated with premarin took nearly twice as long compared to those treated with betamethasone (2.2 months Vs 1.3 months) for resolution of adhesions
Jenkinson SD et al (1984)	Case report	10cases ; 10-22 months of age	Observation alone	In all the cases there was spontaneous separation
Myers JB et al (2006)	Case report	19 cases; 12 to 132 months	Betamethasone cream (0.05%) 1 to 3 courses of twice-daily application for 4 to 6 weeks	successful in treating 13/19 (68%).4 received no treatment, 14 received conjugated estrogen and 1 had surgical lysis before Safe and effective Avoids side effects
Ero lu et al (2011)	Retrospective study	131 cases;	Topical estrogen Topical betamethasone Combined estrogen and betamethasone topical application Each group for 4 weeks	Success with topical estrogen cream only 11/71(15.4%), 5/32 (15.6%) with betamethasone cream only, 5/28 (28.5%) with a combination of estrogen and betamethasone creams. No statistically significant difference between each single agent therapy, each agent with combination therapy or combination therapy with each combined together (relative risk 1.85; 95% confidence interval 0.89-3.89; $P = .11$ ).
Nurzia et al (2003)	Retrospective review	9 cases; 3-6 years	Sharp dissection under general anaesthesia	Patients were with failed medical treatment; 100% success with no recurrence. Edges were approximated with 7-0 chromic catgut
Velander MH et al (2009)	Case report	1 case; 13 months	Topical Conjugated estrogen for 2 weeks Recurrence successfully treated with topical conjugated estrogen for 6 weeks	Failure with betamethasone dipropionate Recurrence after 6 months treated with Topical estradiole caused no effect with significant local irritation
Tutku Soyer (2007)	Prospective study	49 cases; Group -1- 14 months Group-2-14.6 months Group-3- 12.8 months	Group-1:Topical estrogen Group-2:Manual separation (MS) under local anaesthesia Group-3: MS with prophylactic topical estrogen	12/18 (66.6%) separation with 11% (2 patients) recurrence in group-1 12/14 (85.7%) separation with 14.2% (2 patients) recurrence in group-2 17/17 (100%) separation & no recurrence in group-3
Schober J et al (2006)	Retrospective chart review	109 cases; 3 months to 10 years	Topical estrogen treatment	Separation in 79% (85/107), Recurrence in 41% (44/107).21% (22/107) required surgery. (2/21) had recurrent fusion after surgery (10%)
Kumetz et al (2006)	Retrospective study	67 cases; 6months- 14 years	Topical estrogen	Estrogen local application is effective in avoidance of surgery in 35% of patients with persistent or recurrent disease



Bacon et al (2002)	Retrospective chart review	23 cases;	Failure of medical therapy Manual separation	22 of the 23 patients required manual separation. Nine of 23 girls had recurrence of adhesions. Four girls required a repeat manual separation because of recurrent thick adhesions. One of 4 girls required a third manual separation. Five of the 9 recurrences were treated successfully with topical estrogen.
Davis et al (2001)	Retrospective chart review	251 cases; 4 months -16 years	Topical estrogen	Separation in 228 (91%) with local estrogen applied between 2-6 weeks, maximum within 4 weeks(44%); surgery was required

**2.2. Management of labial agglutination in reproductive age women**

Though the incidence of LA in these women is low compared to extremes life (i.e prepubertal or postmenopausal age), cases have been reported in the literature. LA can occur following female circumcision and other skin disorders like lichen sclerosis, herpes simplex, diabetes, pemphigoid and caustic vaginitis. There has also been reports of LA following vaginal delivery and

spontaneous closure during pregnancy.[58] When seen in reproductive age women, it is unlikely to be due to estrogen deficiency.

Literature regarding management in these women is limited favoring surgical management as opposed to medications. Corticosteroids and local anesthetics in addition to surgical separation were beneficial in cases following herpetic infection,[59,60,62] whereas surgical separation only was effective in cases seen in pregnancy or postpartum. [61,63,64][Table-2]

**[Table-2]: Management of Labial agglutination in reproductive age women**

Author (Year of publication)	Cause	No. of patients	Intervention	Comments
Hatim Omar (2000)	Genital herpes	7	Local anaesthetic Surgical correction	5 out of 7 had resolution of symptoms with anaesthetics 2 needed surgical correction
Herieka et al (2001)	Genital herpes	2	Sharp dissection under local anaesthesia Conservative with oral valciclovir, metronidazole, topical lignocaine gel and saline bath	Resolution in both
Seehusen et al (2007)	Postpartum	1	Division under local anaesthesia	Complete recovery in 3 days
Markos AR (2004)	Genital Herpes	1	Topical corticosteroid	Separation without residual effect Manual separation under local anesthesia was unsuccessful
Uei T et al (2000)	Unknown	1	Dissection under lumbar anaesthesia	Separation without recurrence
Kucuk M et al (2011)	Unknown Occurred during pregnancy	1	Surgical correction	Complete resolution

**2.3. Management of labial agglutination in postmenopausal women**

Though not very common, it is not unusual to see labial fusion in postmenopausal women. Estrogen deficiency plays a major role in labial fusion by making it susceptible to injuries. Furthermore, it is more likely for carcinoma vulva or vagina to occur in this age group than the others. In presence of symptoms other than that is expected for labial fusion, e.g pruritus, secondary causes should be sought. Most of the women present with urinary symptoms like

incontinence following retention in the pouch [65-69] and recurrent UTIs. Ascending infection can even rarely present as pyosalpinx. [70]

Separation of labial agglutination is done by manual separation [Figure 5, 6, 7] or surgical dissection in these women to relieve the symptoms. Other associated complications like pyosalpinx (if present) can be managed at the same time. Postoperative use of topical estrogen helps in prevention as well as treatment of any further recurrence. [65]



**Figure-5: Labial agglutination in a postmenopausal women [original]**



**Figure-6: Manual separation using a metallic sound [original]**



**Figure-7: Vulva after separation [original]**

### 3. Recurrent Labial Agglutination

Recurrence of agglutination in previously treated cases of LA is significant and it seems to be independent of the method used for separation. The reported rates vary between 14% and 41% in different studies. [7,21,47,49,55,56,57,71]

Recurrence can be seen after treatment in all the age groups. In a study involving 48 cases with recurrence, it was found that 83% of recurrences were following Topical estrogen use alone and in 14% patients the recurrence was following manual separation with or without topical estrogen.[55]

The raw area after separation poses high risk for recurrence. Subsequent agglutinations occurring after a surgical separation, are usually dense and tough. [72]

While the best treatment for recurrence is yet to be standardized, Topical estrogen appears to be effective as a first line treatment in recurrences occurring after surgery. In a study it was seen that Topical estrogen could prevent surgery in 35% of cases where recurrence followed earlier manual separation. [55] [Table-3]

**[Table-3]: Management of Recurrent Labial agglutination**

Author (Year of publication)	No. of cases	Modality	Comment
Capraro VJ et al (1972)	10	Topical estrogen	Complete separation in 60%(6/10) cases
Velander MH et al (2009)	1	Topical estrogen	
Schober J et al (2006)	44/107 recurrence 2 had recurrence after surgery	22 cases topical estrogen 22 cases required surgical separation	Estrogen was not helpful in separation in cases where there was recurrence after surgery
Kumetz LM et al (2006)	48	Surgery in 5 cases due to urinary symptoms Topical estrogen in 43 cases	15 /43 had separation, 9 required surgery Topical estrogen was successful in preventing manual separation in 2 out of 5cases where previous manual separation was done
Bacon JL (2002)	primary medical failure 9/23; recurrence after manual separation	2 cases no treatment 4 cases topical estrogen Repeat manual separation	1 required 3 <sup>rd</sup> separation

While it is a good practice to maintain good vulvar hygiene and elaborated recommendations like frequently changing of diapers, use of cotton only underwear, perfume free soaps ,practicing front to back wiping, limiting deodorant and bubble baths have been made earlier; in a recent study involving 110 patients it was found that there is no correlation between recurrence of labial fusion with factors like body weight percentile, frequency of diaper change, frequency of diaper dermatitis, hygiene products used, presence of infection, presence of allergy, mother's use of oral contraceptive drugs before pregnancy, or presence of any pathology in other family members.[73]

#### **4. Surgical technique**

Surgical separation of LA is done in different situations. Though done mostly for cases where medical therapy and manual separation fails or there is a recurrence, it has been used as primary modality in cases with severe urinary symptoms and significant parenteral anxiety.

Most common indications for surgery are failure of medical treatment (13 out of 23), followed by demand by parents, reaction to cream and urinary obstruction. It was also seen in a study that surgical interventions were more likely to be required in children over 6 years of age even after prolonged medication. [57]

Standard surgical method involves sharp dissection under anaesthesia. Several methods are employed to decrease chances for recurrence including split-thickness skin grafts. In nine cases, only reapproximation of the edges with 7-0 chromic catgut was tried and no recurrences were reported by 8.6 months follow-up.[50] Other studies reported successful use of acellular dermal allograft and even cutting seton with postoperative topical clobetasol to prevent recurrence in cases with agglutination following lichen planus and squamous cell carcinoma of vagina. [74,75]

Pieces of saline infusion tubes and amniotic membrane were sutured to the raw area after separation successfully in few other studies to prevent further recurrence. [29,51]

#### **5. Conclusion**

- Careful and systematic physical examination of vulvar area is the key to correct diagnosis of cases with vulvar agglutination and helps in eliminating other differentials.
- In asymptomatic prepubertal girls, maintaining good vulvar hygiene, treating vulvovaginitis and conservative expectant management till natural onset of puberty should be done. These girls should be followed up with regular screening for asymptomatic bacteriuria.
- There is lack of uniformity in the studies regarding the frequency and duration of topical estrogen treatment. The possibility of inadequate duration of treatment contributing to reported

failure of therapy cannot be ruled out. Taking into account the evidence by published literature, it is recommended that twice application of conjugated estrogen for at least 4 to 6 weeks should be done. If there are evidences of separation, treatment can be extended upto 3 months in absence of side effects. There is no role for oral estrogen therapy.

- If there are no evidence of separation at end of 6 weeks, it should be considered as failure of topical estrogen treatment.
- Side effects are mild with topical estrogen treatment and are limited to breast pain or tenderness, headache, hair loss, mild nausea or vomiting, spotting or breakthrough bleeding, stomach cramps or bloating. These are reversible after stoppage of treatment.
- If side effects are bothersome, Topical estrogen should be stopped and alternative form of treatment should be employed.
- Data regarding use of topical betamethasone is inconclusive and can be considered in cases with no separation using estrogen.
- Manual separation of labia under short duration general anesthesia in an operating room set up should be employed when topical estrogen therapy fails.
- When surgical separation is required, sharp dissection should be done to separate adhesions.
- Women in reproductive age group with labial agglutination need surgical separation as a primary modality. Maintaining local hygiene, local anesthetics and saline bath should be practiced especially in cases with infectious causes like herpes genitalis to avoid agglutination.
- Postmenopausal women respond best to manual separation with postoperative topical estrogen therapy. Surgical separation should be done in cases with failure or recurrence.
- To prevent recurrence, maintaining good vulvar hygiene and use of bland ointment after separation are potentially beneficial and should be practiced. Use of topical estrogen following separation is favored.
- In cases with recurrence after a primary surgical separation, any of the methods like suturing, acellular graft or saline infusion tubes can be used to prevent further recurrence.

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