Inverted Papilloma: Experience at Allama Iqbal Medical College and King Edward Medical College

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Purpose: In this study, the surgical management of an inverted papilloma of the nose and paranasal sinuses at our institutions (Allama Iqbal Medical College and King Edward Medical College Lahore-Pakistan) is reviewed. **Methods:** Nine patients diagnosed with an inverted papilloma and treated at the Ear Nose and Throat Departments of Allama Iqbal Medical College and King Edward Medical College Lahore-Pakistan from 1995 to 2003 were retrospectively reviewed. One patient after the complete work up left without surgery. Eight patients were treated with lateral rhinotomy and medial maxillectomy. **Results:** The patients had a mean follow up of 4 years and eight months (8 years to 2 years 3 months).The overall recurrence rate was 12%. The patient with recurrence on biopsy showed presence of squamous cell carcinoma. **Conclusions**: All unilateral nasal masses must be biopsied.Lateral rhinotomy with medial maxillectomy is an effective way of treating sinonasal inverted papilloma in our set up.

Key words Inverted papillomas, :

Inverted papilloma is a benign sinonasal lesion constituting 0.5% to 4%of all nasal tumors[1]. In 1855 Ward reported a case of nasal papilloma although Billroth is usually credited with the first description of a true papilloma of the nasal cavity. The tumor was more specifically characterized by Ringertz in 1938 as one with a propensity for locally invading the surrounding tissues and for recurrence[2]. Squamous cell carcinoma (SCC) arising in inverted papilloma has been reported in the literature for more than 30 years and has a reported incidence between 5%and 13%[3].

Inverted papilloma is of epithelial origin and is characterizd by a hyperplastic epithelium with an endophytic type of growing, while the basement membrane is intact and morphologically normal. It is important that an inverted papilloma is removed in entirety if only to ensure that patients are not subjected to repeated surgical interventions over a number of years. Of the surgical approaches to this neoplasm which has evolved over the past century, the generally accepted standard is medial maxillectomy through an external incision .Medial maxillectomy is en bloc resection of the party wall between the nasal cavity and antrum and adjacent ethmoid labyrinth. It provides removal of the area into which tumor extends[4].

In this study we reviewed 9 patients affected by an inverted papilloma who were treated from 1995 to 2003 in our institutions.

Materials and methods:

This study consists of patients of sinonasal papillomas managed in the period from 1995-2003 at Allama Iqbal Medical College and King Edward Medical College Lahore-Pakistan. All patients were preoperatively evaluated by plain films and biopsy. Computerised tomography was obtained whenever possible. Patient demographics, clinical features, any previous surgery, extent of tumour at the time of presentation were recorded. All the lesions were staged according to the staging system as proposed by Krouse, 2000. One patient after the complete work up left without surgery. Eight patients were treated with lateral rhinotomy and medial maxillectomy. Maximum follow up was 8 years and minimum follow up was 2 years and 3 months.

Results:

Over a period of 8years from 1995 to 2003, nine cases of inverted papilloma were managed. There was a male predominance with a male to female ratio of 7:2. Clinical features of patients are shown in Table –1. Computerised tomography could be obtained in 7/9 patients. Staging of lesions as suggested by Krouse 2000 is shown in Table 2.There was no patient with concurrent malignancy in the series. Three of the nine patients had undergone previous surgery (intranasal polypectomy-2 cases and lateral rhinotomoy –1 case) with recurrent lesions.

One patient after the complete work up left without surgery. Eight of our patients underwent madial maxillectomy through an external approach. All patients developed crusts which needed periodic removal. One patient developed maggots and orbital cellulitis during the follow up period which was managed. One of our patients showed recurrence along with presence of squamous cell carcinoma after undergoing medial maxillectomy and refused any further treatment.

Krouse's Staging System for Inverted Papilloma[16]

- T1 Tumour totally confined to the nasal cavity,without extension into the sinuses.The tumour can be localised to one wall region of the nasal cavity,or can be bulky and extensive within the nasal cavity, but must not extend into the sinuses or into any extranasal compartment.There must be no concurrent malignancy
- T2 Tumour involving the ostiomeatal complex, and/or the medial portion of the maxillary sinus,with or

without involvement of the nasal cavity. There must be no concurrent malignancy

- T3 Tumour involving the lateral, inferior, superior, anterior, or posterior walls of the maxillary sinus, the sphenoid sinus, and/or the frontal sinus with or without involvement of the medial portion of the maxillary sinus, the ethmoid sinuses, or the nasal cavity.There must be no concurrent malignancy
- T4 All tumours with any extanasal /extrasinus extension to involve adajacent , contiguous structures such as the orbit, the intracranial compartment, or the pterygomaxillary space.All tumours associated with malignancy.

Table I Clinical Features

Nasal Obstruction	9
Nasal Mass	9
Proptosis	2
Epistaxis	3

Table II Staging Krouse's 2000

T2	2
T3	6
T4	1

Discussion:

Schnederian papillomas are ectodermal lesions arising generally from the lateral nasal wall. These are ominous lesions because of their high recurrence rate (50%), risk of malignant transformation (5-15%), tendency towards multicentricity and local aggressiveness.

The sinonasal inverted papillomas have been reported in all age groups from adolescence to middle or old age with a typical peak incidence in the fifth or sixth decade of life. Age range in our series was 30-70 years with an average age of 50 years. The sex ratio of patients in our series revealed a male predominance of7:2 which is in accordance with the literature but is an unsolved mystery.

The optimum management of inverted papilloma commences with early diagnosis of the condition. Clinicians should have a low threshold of suspicion for the condition and biopsy all unilateral lesions of the nose. Two of our patients had undergone intranasal polypectomy at other centers without submitting the removed material for histological examination. Computerised tomography remains the imaging modality of choice. It was economic constraints at times which do not allow us to get C T scan in all patients.

Surgery is the agreed primary modality of choice. Limited surgery such as conventional polypectomy is associated with recurrence rate of up to 75 per cent .This has led most authors to recommend aggressive open surgical procedures i.e. lateral rhinotomy with enbloc resection of the tumor and medial maxillectomy. This has been accompanied by low rcurrence rates of between zero and 29 per cent[5] .We noted recurrence in one patient which also had associated squamous cell carcinoma on histopathology.

Since 1990, with the rapid expansion of endoscopic sinus surgical techniques, a number of otolaryngologists have begun to treat inverted papillomas with intranasal endoscopic approaches[6,7]. In the evaluation of surgical approaches to diseases it is important to account for the differences in the severity of the disease. To accurately determine treatment outcomes an assessment of the preoperative extent and nature of the disease is critical. For this reason, staging systems are an essential aspect of the evaluation process in various inflammatory and neoplastic processes, including inverted papilloma. Patients in this series were staged according to the staging system for inverted papillomas as suggested by Krause –2000. One of our patients had disease extending into the orbit and was thus staged as T4.

Incidence of squamous cell carcinoma with inverted papilloma is 5 % - 13%. None of our patients showed concurrent malignancy. We noted recurrence in one patient which also had associated squamous cell carcinoma on histopathology.

Crusting within the nasal cavity was troublesome in the immediate postoperative period but subsided with time. One of our patients developed maggots in nose and ethmoids with orbital cellulitis. No other complication was observed.

Conclusions:

1. Always biopsy a unilateral nasal mass.
2. Inverted papilloma is a benign but locally aggressive sinonasal lesion.
3. Surgery is the agreed primary modality of choice.
4. Inverted papilloma is best treated with lateral rhinotomy and medial maxillectomy in our set up.

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Prescribing in Pregnancy

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Objective: To assess the prescribing patterns and clinical practices in the use of pharmaceutical agents in pregnancy **Study Design:** Observational, Cross-sectional study. **Study Period:** March 2002 to March 2003 **Setting:**Study was conducted at antenatal clinic, Jinnah Hospital, Lahore. **Materials and Methods:** 250 patients from antenatal clinic were interviewed to collect information regarding age, parity, gestational age, any medication, its indication, route, duration and prescriber during current pregnancy on a pre-designed proforma. **Sampling Method:** Patients were enrolled in this study on first come and enroll basis. **Results:** Most of the women (90%) visiting the antenatal clinic were in the age group 21–30years. 94% of the women were taking medications and the prescriptions included haematenics (88%), folic acid (61%), calcium supplements (63%), antibiotics (22%), anti-fungals (19%), antiemetics (8%) and laxatives (6%). 6% of women were not taking any medication. Commonest prescribers were general practitioners (46%). Rest of the prescribers were medical officers at antenatal clinic (28%), LHVs/nurses (11%) and specialists (9%). Self-medication was seen in 6%. 47% of the women taking self-medications were among the educated group (Matric and above) and 53% of the women were among the uneducated group ($P < 0.001$). 28% took treatment from general practitioners and lady health visitors without any certain diagnosis, on symptomatic grounds. **Conclusion:** The use of drugs in pregnancy is substantial and varied. Information on the use of drugs during pregnancy is scarce and anecdotal. Careful consideration of the benefits to the mother and risks to the fetus is required, when prescribing drugs during pregnancy. All prescriptions or drugs recommended in pregnancy must have solid evidence derived from current literature.

Key Word: Drugs, Pregnancy, Prescriptions, antenatal

Pregnancy is a time of profound physiological change in a women's body. Affecting almost every organ system. These unique changes challenge clinicians managing disease states during pregnancy and affect the selection of medications. Drug therapy may need to be adjusted due to the unique pharmacokinetics of pregnancy as well as to account for teratogenetic concerns[1].

Thalidomide, a drug prescribed to women during 1960s as an antianxiety medication let to the birth of thousands of grossly malformed infants[2]. This catastrophe still makes clinician uneasy whenever they are faced with prescribing a new medication to a pregnant woman. In the case of thalidomide, it took several years before the causal effect was actually realized. In the US, this led to the creation of drug regulations, designed to help endure the safe use of prescribed medications.

When considering drug therapy in pregnancy, the risk of treatment for the fetus has to be weighed against the risk to the mother and the child of carrying out no treatment. However, carefully selected drugs and closed meshed monitoring may even decrease the risk for the child[3].

Throughout pregnancy drugs may affect fetal growth and functional development. Teratogenetic risk to the fetus is highest in the 1st trimester, as it is the period of organogenesis. Exposure to teratogens can expose a developing fetus to major congenital malformations. All orally administered medication enter the fetal circulation and therefore no medication should be considered completely safe. Ethical consideration makes prospective placebo-controlled, double-blinded studies impossible, so most information that has been gathered about the effects of medications and other therapeutics on a fetus has been collected retrospectively[4].

Each year, almost four million women in the US give birth and nearly 15% of these women have used a legal drug, either prescription or non-prescription, within 6 months of conception. An astonishing 75% of these women were using 3-10 drugs[5]. Nearly 62% of all pregnant women received at least one drug, 25% took an opiate and 13% took a psychotrophe.

Drug therapy is a highly specialized field. In pregnancy even an educated women is dependant on the advice of a health care provider[6]. The most frequent medical intervention performed by a doctor is writing of a prescription and he or she has the freedom to prescribe whatever drugs they deem necessary[7,8].

The healthcare cost in the general and drug cost in particular arising every where and most of the increased cost of drugs throughout the world is due to use of new medicines[9] and Pakistan is no exception. Although new is not necessary, better. Many clinicians continue to prescribe the new and the more expensive drugs as first line therapy[10]. Scarce financial resources are spent on unnecessary nutritional supplements mostly by prescribing vitamin preparations and nearly half of prescribed medicines in pregnancy are tonics and antacids. Laxatives, antibiotics, analgesics and anti-emetics are second in this list. Routine addition of multivitamin in prescription contributes to polypharmacy[11] as well as to raising the cost of prescribed drugs[12]. This study was design to assess the prescribing practices and prescribers during pregnancy and to evaluate the implementation of such practices.

Results:

The age and parity of study group is as in table I. The educational and social status is as in table II. Most of the women (90%) visiting the antenatal clinics were in the age group 21–30years. The prescriptions included haematenics (88%), folic acid (61%), calcium supplements (63%), antibiotics (22%), anti-fungals (19%), antiemetics (8%) and laxatives (6%). 6% of women were not taking any medication. The supplements used are as in table III. Commonest prescribers were general practitioners (56%). Rest of the prescribers were medical officers at antenatal clinic (32%), LHVs/nurses (19%) and specialists (9%). Self-medication was seen in 6%. 47% of the women taking self-medications were among the educated group (Matric and above) and 53% of the women were among the uneducated group ($P < 0.001$). 28% took treatment from general practitioners and lady health visitors without any certain diagnosis on symptomatic grounds.

Among 250 patients, 220 (88%) took elemental iron mainly in a dose of 50-100mg/day (178 patients, 71.2%) 24 patients (9.6%) took iron in <50mg/day and only 18 patients (7.2%) took iron in therapeutic doses that is >100mg/day. 11 patients (4.4%) took injectable iron because of poor compliance. Calcium, folic acid and multivitamins containing high potency B-complex were taken by 158 patients (63.2%), 153 patients (61.2%) and 144 patients (57.6%) respectively.

The injectables used in pregnancy are as in table IV. Oral and injectable antibiotics mainly in penicillin group (29 patients, 11.6%) were employed. Oral antibiotics prescribed in pregnancy are as in table V.

Discussion:

Maternal and fetal effects of most therapeutic agents are unknown for about one half of medications. However, the majority of pregnant women (40% to 90 %) are exposed to medications during pregnancy. These include a variety of agents: Vitamins, minerals, antibiotics, laxatives, antiemetics, sedatives, antacids and antihistamines[13,14]. Many medications are taken without physicians' advice or before recognition of pregnancy[15].

The incidence of medication use during pregnancy is high. Of over 250 pregnant women surveyed, approximately 94% took medication prescribed by a health care provider. Results of the study showed that pregnant women were prescribed by general practioners (56%), medical officers of a teaching (Jinnah) hospital (32 %), specialists (9.2 %), nurses/ LHVs (19.2 %). It was also seen that a small but significant (6 %) proportion took drugs with out medical advice. This is a worrying trend as these patients also have a tendency to hide this fact for the fear of rebuke. This may signify a higher proportion of such practices without the medical rationale and advice. Physicians must discuss use of drugs and its dangers with their patients to dispel such practices. At the same time in a largly anaemic population like that of Pakistan a similar figure (6% of the study group) were not taking any medicine. This means either lack, inability or refusal to follow medical advice regarding haematinics. In a 1987 survey of nearly 500 pregnant women 10 % of them reported that they took neither prescriptions or over the counter drugs. The incidence of medication used during pregnancy seems considerably lower in United Kingdom compared to that in the United States. In one report, fewer than 10 % of pregnant women in the United Kingdom took medication other than Prenatal Vitamins and iron supplements during first trimester[16]. How ever, this showed a high rate of drugs taken by antenatal pregnant women. 88% took haematinics, 63% took calcium supplements 61% folic acid. 22% took various types of antibiotics, 18.8% received analgesics 8% antiemetics and 6% laxatives. 6% received no treatments and there were self-medications in 6%.

All the drugs are chemical poisons and they must be used with utmost care in pregnancy. The irrational use of drugs by both prescriber and consumer is infact a global problem, which can be assessed by a standardized method of prescription analysis. For this purpose WHO have recommended minimum five core indicators, which can give an idea about the quality of a prescription and provide uniform parameters for comparative analysis of prescriptions collected from various health care facilities/ countries. These parameters include the number of drugs per-prescription and percentage of generic drugs, antibiotics, injections and drugs from national essential drug list in a total analyzed prescriptions[17].

Infection occurs commonly during pregnancy and it may be necessary to prescribe antimicrobial agents. Antibacterial are among the most frequently prescribed medications during pregnancy. Most of these drugs are safe for use during pregnancy. Antibiotic may be associated with adverse fetal effects. All the penicillins are apparently safe for use during pregnancy in patients not allergic to these drugs. More recently developed broad spectrum penicillins and those combined with the beta lactamase inhibiters such as clavulanic acids and salbactum have not been adequately studied during pregnancy. However a significant risk for adverse effects seems unlikely. All the penicillins cross the placenta resulting in significant fetal levels[18]. Thus the penicillines are the drug of choice in pregnancy. All cephalosporins cross the placenta to a similar degree resulting in significant levels. Eryothromycin, a macrolide antibiotic is not associated with adverse fetal outcome or congenital anomalies. This agent does not cross placenta in appreciable quantity[19]. All aminoglycosides cross the placenta to the same degree[20,21] and result in significant fetal levels. A drug in this class streptomycin has been reported to be associated with 8th cranial nerve damage in fetuses whose mother received it for a significant time during pregnancy[22,23]. Nitrofurantoin is another agent use to treat urinary tract infections during pregnancy. This drug was not associated with an increase risk of congenital

anomalies in one study and there were no reports of adverse effects following its use during pregnancy[24]. The flouroquinolones a re r elatively new a ntibiotics frequently used to treat U.T.I. There are no studies of congenital anomalies in infants whose mothers took these drugs during p regnancy. I n this s tudy 2 2% o f p regnant women took various type of antibiotics. Among them most common was ampicillin.19.2% used local antifungal. Most of the patients took antibiotics for urinary tract infection (35%) and upper respiratory tract infection (21%).

Analgesics are the medication most commonly prescribed to the pregnant women. With few exceptions most analgesics can be administered to pregnant women with relative safety. In this study 18.8% of pregnant women took analgesics on symptomatic grounds. Most of these prescriptions were prescribed by paramedical staff including nurses, lady health visitors and also by self-medication.

Drugs taken by pregnant women could have profound effect on pregnancy outcome for both the mother and the fetus. In developing countries like Pakistan drug regulation is poor, access is unrestricted and abuse of drugs especially antibiotics is rampant. This study was undertaken to determine the pattern and extent of drug consumption amongst pregnant women at Jinnah Hospital Lahore. Of the 250 patients interviewed 94% took at least one drug during pregnancy. Many of them used a median # of 2 to 3 drugs, Iron (88%), Folic acid (61%), and calcium (63%). Similar result was collected from a study, which was conducted on Italian women. Iron deficiency anemia is common among pregnant women in developing countries. So this high rate of supplement therapy is cost effective in Pakistan.

Our present study, when compared with similar studies previously conducted by others confirms that variations in prescribing practices do exist in different areas of the world. Measures should be taken to make prescriber cost conscious through continued unbiased educational programs as the educational interventions have been shown to be effective in favorable in changing the patterns of drug prescriptions..

Table I Age and parity Distribution

Age in years	Parity		
	Primigravida	Multigravida	GrandMultigravida
< 20	2 (0.8%)	-	-
21–30	82 (32.8%)	138 (55.2%)	2 (0.8%)
31-40	1 (0.4%)	20 (8.0%)	4 (1.6%)
> 40	-	-	1 (0.4%)

Table II Education and Social Status of Subjects

Education	Social Status		
	Lower Class	Middle Class	Upper Class
Uneducated	94 (37.6%)	-	-
Primary	26 (10.4%)	12 (04.8%)	-
Matric	13 (05.2%)	67 (26.8%)	-
Graduation	-	32 (12.8%)	-
Higher	-	06 (02.4%)	-

Table III Supplements Distribution

Haematinics (mg/day)			Multivitamins			Calcium
<50	50–100	>10	Folic Acid	High potency B- complex	Fat Soluble Vitamins	
24 (9.6%)	178 (71.%)	18(7.2%)	153(61%)	144(57.6%)	86(34%)	158(63%)

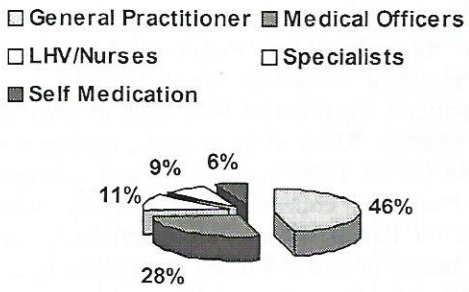
Table IV Injectables Used in Pregnancy

Injectable Iron	I/V Fluids	Anti-emetics	Injectable Antibiotics	Tetanus toxoid
11(4.4%)	04(1.6%)	01(0.4%)	01(0.4%)	84 33.6%)

Table V Oral antibiotics used in pregnancy

Penicillins	Cephalosporins	Macrolides	Tetra-cyclines	Quinolones	Sulfon-amides
29 (11.6%)	06(2.4%)	07(2.8%)	-	12(4.8%)	-

Figure I Prescribers in the Study



Conclusion:

Information on the use of drugs during pregnancy is scarce and anecdotal. Careful consideration of the benefits to the mother and risks to the fetus is required, when prescribing drugs during pregnancy. All prescriptions or drugs recommended in pregnancy must have solid evidence derived from current literature.

It is a major clinical and Public health problem that there is no clear strategy as to how we can make the best use of information obtained when pregnant women use drugs. For this reason, some pregnant women are not treated as they should be and some are given drugs they should not use. So

- Drugs should be prescribed for a pregnant woman only when the indications are clear and specific, and the expected benefit to the mother is greater than the risk to the fetus.
- If possible avoid all drugs in the first trimester.
- Prescribe drugs that have been well tried in pregnancy in preference to newer preparations.

Use the smallest effective dose for the shortest therapeutic time

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