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Original Research Article

Clinical presentation of autoimmune disorders in pregnancy

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ABSTRACT

Background: Autoimmune disorders have a significant impact over the health of an individual. This heterogenous group of disorders affects pregnancy in a multitude of ways. Pregnancies with autoimmune disorders are usually cared for by a multidisciplinary team of doctors.
Methods: Pregnancies with autoimmune disorders were studied over a one-year period in one unit of a medical college teaching hospital set up. Obstetric and neonatal outcomes were studied.
Results: Ten patients were studied. Average age was 29.9 years. Majority presented in early second trimester. Eight patients were ANA positive. Two patients had antiphospholipid antibody syndrome, for whom low molecular weight heparin was helpful. Hypothyroidism was seen in two patients. Bad obstetric history was seen in most patients. Successful neonatal outcome was seen in six patients. One patient had Evans syndrome. There were no maternal mortalities. There was one perinatal mortality.
Conclusions: Autoimmune disorders in pregnancy when managed in a tertiary care centre with multidisciplinary approach can result in good obstetric and neonatal outcomes.

Keywords: ANA positivity, Aspirin, Autoimmune disorders, Heparin, Pregnancy

INTRODUCTION

In pre-eclampsia, the prevalence of autoimmune disorders in the general population is around 3% to 7%. The prevalence of this group of disorders is probably underestimated and is more common in females.[1]

Systemic lupus erythematosus has various manifestations, the pathognomonic investigation being ANA positivity. In the context of pregnancies with autoimmune disorders, ANA positivity is a common feature.

Many of these patients are otherwise asymptomatic apart from abortions or pregnancy associated hypertension. Few patients have more than one auto-antibody positive. Moreover, the occurrence of Antiphospholipid antibody syndrome in SLE is also well described. In the Indian context, Singh et al have described a 25.3% prevalence of APS in SLE. They have also described the increased morbidity that these women experience and the high disease burden associated with the autoimmune disorders in pregnancy.[2] An analysis of ten cases of autoimmune disorders in pregnancy and discussion of various features is attempted below.

METHODS

A prospective observational study was conducted in a single unit in the department of obstetrics and gynaecology in a tertiary care hospital. All patients who were diagnosed cases of autoimmune disorders and underwent medical care, antenatal and care and delivery in the department were studied.

The study was conducted over one year. The case files were studied and details of medical and obstetric outcomes were studied (March 2016 to February 2017). All medical outcomes such as time of onset of disease, medications which the patient was on, need for admission and any medical complications were noted. Maternal and foetal outcomes including gestational age at delivery, birth weights, problems during labour and neonatal outcomes were studied in detail.

RESULTS

The number of patients who delivered in the study period was 1056. During this period, 10 patients of autoimmune diseases were managed. The details of the patients are presented here.

Case 1

A 30 year old married woman for 4 years G3A2 registered in our outpatient department at 20 weeks of gestation. Evaluation for bad obstetric history revealed IgM ACLA positive status. She was started on low molecular weight heparin 0.6 cc subcutaneous twice a day and tablet Aspirin 150 mg once a day. She required one admission at 33 weeks of gestation in view of threatened preterm labour. She was given injectable steroids and tocolytics till completion of steroids. At 37 weeks of gestation pre-induction ripening of cervix by Foley's catheter was done and she delivered vaginally a female child of 2.882 kg with Apgar score of 9/10.

Case 2

A 35 year old married woman for 17 years G2A1 presented at 6 weeks of gestation with bleeding per vaginum. Blood pressure was 200/120 mm Hg with no albuminuria. Investigations showed anti-SSA antibody positivity and ANA positivity. Rheumatology reference was taken and she was started on once a day tablets of dexamethasone 4 mg, HCQS 200 mg and aspirin 75 mg. Tablets Alpha methyldopa 250 mg thrice a day and Nifedipine 10 mg twice a day were started for blood pressure control. IgM HSV was positive (which had been performed few days prior to initial presentation of to our hospital) for which she was started on tablet acyclovir 200 mg twice a day.

At 36 weeks of gestation she complained of generalised itching and alkaline phosphatase was found to be elevated. There was marginal improvement with ursodeoxycholic acid 300 mg twice a day.

Serial antenatal ultrasonography showed appropriate for gestational age with an estimated birth weight of 2.4 kg prior to induction. At 38 weeks of gestation, induction of labour was done and there was no intrapartum fetal distress. Emergency lower segment caesarean section was done in view of failure of induction and she delivered female child of 1.59 kgs with Apgar score of 2/10 and 9/10. Baby was shifted to NICU and required ventilation but expired on day 2 of life due to multi organ failure.

Case 3

A 35 year old woman married for 6 years G3P1L1A1, a known case of rheumatoid arthritis (RA factor positive) and hypothyroidism, presented at 8 weeks with threatened abortion.

Her first pregnancy was a second trimester abortion at 5 months of gestation, of which no details were available. In her second pregnancy, cervical encirclage was done at around 5 months of gestation and the pregnancy resulted in vaginal delivery of live born child at 9 months.

In the current pregnancy; she had a dichorionic diamniotic twin gestation. She was started on injectable progesterone support 500 mg once a week. She was continued on once a day tablets of hydroxychloroquine (HCQS) 300 mg, aspirin 75 mg and levothyroxine 25 microgram. Biochemical markers for aneuploidy were negative. At 18 weeks, ultrasonography showed cervical length of 1.6 centimetres (cms) and McDonald's cervical encirclage procedure was done. However, she came with complaints of pain in abdomen at 22 weeks of gestation. She was admitted in view of preterm labour. Tocolytic drugs were started but pregnancy could not be salvaged and she aborted fetuses of 480 and 490 grams respectively.

Case 4

A 32 year woman married for 4 years G3P2 IUFD2 registered at 12 weeks of gestation. Her previous pregnancies were intrauterine fetal demises, one at 8 months and other at 6 months of gestation, with history of high blood pressure in both. Investigations showed LA and IgG ACLA positive. Injection LMWH 0.6 cc subcuteneous and tablet aspirin 150 mg once a day were started. She followed up regularly and fetal surveillance was optimum. Labour was spontaneous and she progressed normally at 37 weeks and she delivered a male child of 2.8 kgs with Apgar score of 9/10.

Case 5

A 30 year old woman married for 12 years G4P3L1NND2 known case of SLE presented at 22 weeks of gestation and was found to have anaemia with haemoglobin of 5.6 gm%. After ruling out other causes, oral haematinics were initiated. Tablet aspirin 75mg once a day was continued, and rest of pregnancy was uneventful. Labour progressed spontaneously and she delivered male child of 2.9 kgs with Apgar score of 9/10.

Case 6

A 23 year old woman married for 2 years primigravida registered at 26 weeks of gestation, and auscultation fetal

heart sounds with doppler showed irregularity. Initial impression was fetal arrhythmia and a fetal echocardiogram was ordered and autoimmune profile was sent. Though fetal echocardiogram did not confirm fetal arrhythmia, ANA turned out to be positive in the titres of 1:320 (coarse speckled).

History was reviewed, and she did not report joint pains, photosensitivity, oral ulcers or other symptomatology of SLE. Rheumatologists advised C3, C4, 24-hour urine protein, anti SSA and anti SSB; which were all negative. She was started on aspirin 75 mg OD. At 41 weeks of gestation, induction of labour by Foleys catheter was done. Emergency LSCS was done in view of fetal distress and she delivered male child of 2.868 kgs with Apgar score of 9/10.

Case 7

A 27 year old woman married for 5 years G2P1L1 at 29 weeks of gestation. She went to private practitioner with complaints of generalized swelling and rash over the body, oral ulcers and fever with chills for 10 days. She had been investigated prior to presentation here and had haemoglobin of 9.6 gm%, whole blood count of 25000/ cu mm, platelet count of 28000/cu mm and ANA positivity (1:1000 titres). She had received 2 units of single donor platelet transfusion and had been started on steroids, antibiotics, intravenous fluids, anti-histaminics, anti-malarials and then was referred here.

At admission, oral ulcers were present, rash was present over the malar area and abdominal examination showed 28 weeks gestation suggestive of IUGR. Whole blood count improved to 10,600 but platelet count dropped to 20000/ cu mm. Viral markers were negative but SGOT was elevated (189 IU/ml) though SGPT was normal (31 IU/ml). CRP was elevated (19.5), dsDNA was positive, C3.C4 were within normal limits, c-ANCA and p-ANCA were negative and U1SNRNP was strong positive (+++). 24-hour urine protein was elevated (1158 mg) and lipase was elevated (10618 U/ml). Serum TSH was 5.47 U/ml. The clinical impression was one of mixed connective tissue disorder with autoimmune haemolytic anaemia with thrombocytopenia, autoimmune pancreatitis, thyroditis and nephropathy.

Haematology reference was taken and she was started on tablet prednisolone 1mg/kg, tablet azathioprine 50 mg OD. It was further advised to give intravenous immunoglobulin or 6 units of random donor platelets (RDP) or 1 SDP transfusion; if patient goes into labour or bleeding from any site. She was also started on tablet HCQS 200 mg twice a day. She went into inevitable preterm labour at 34 weeks of gestation and delivered a female child 1.13 kg with Apgar score of 9/10. Baby was shifted to NICU in view of low birth weight. 6 units RDP transfusion and one whole blood transfusion were given to the mother peripartum.

Rest of postnatal course was uneventful, and steroids were tapered. Platelet counts improved and proteinuria normalised. Neonate was discharged after 10 days of NICU stay.

Case 8

A 31 year old woman married for 12 years with a precious pregnancy G2IUFD1 complaining of bleeding per vaginum for 2 months for which she required 4 admissions between 8 to 14 weeks of gestation. Ultrasonography was done which was suggestive of single live intrauterine gestation of 15.6 weeks with no evidence of retroplacental clot and she was started on injectable progesterone support weekly, injection tranexemic acid, and injectable antibiotics and was discharged after 6 days. She again complained of bleeding at 19 weeks of gestation and was referred here in view of bleeding per vaginum and ultrasonography was suggestive of a cervical canal hematoma of 7.2x4.6 cms.

At the time of admission, uterus corresponded to 22 weeks size, on per speculum there were no lesions on cervix, minimal bleeding was present and on per vaginum examination os was closed. Investigations showed ANA positivity in the titres of 1:60. She was started on injection tranexemic acid, weekly progesterone support 500 mg, aspirin 75 mg but she aborted at 23 weeks of gestation male child of 430 grams.

Case 9

A 31 year old woman married for 8 years G3P1L1A1registered at 13 weeks of gestation. She was diagnosed with multiple connective tissue disease one year prior to conception when she complained of joint pain, malar rash and photosensitivity. She was ANA positive and U1 SNRNP strong positive; while RA, anti-ds DNA, anti-SSA, anti-SSB, APLA, anti-Beta2 glycoprotein were all negative. She was on prednisolone, HCQS 300 mg OD and aspirin 75 mg once a day. Patient was also a known case of hypothyroidism on levothyroxine 100microgram OD. Conception was spontaneous and antenatal care was regular. Pre-induction ripening of the cervix with foleys catheter WAS done at 40 weeks of gestation. Labour was covered with intravenous hydrocortisone. She delivered male child of 3.174 kg with Apgar score of 9/10.

Case 10

A 25 year old woman married for 5 years G2A1 with 2 months of gestation, recently detected to be pregnant by a positive urine pregnancy test, presented with spotting per vaginum. Ultrasonography showed missed abortion of 8 weeks for which suction and evacuation was needed. Investigations showed ANA positive status in the titres of 1:160(+4), and patient is being followed up for further evaluation.

Table 1: Brief summary of the cases.

Age	Weeks at diagnosis	Previous poor obstetric outcome	Autoimmune disorder	Medical disorders	Treatment	Obstetric	Fetal outcome
30	20	Yes	IgM-aCLA +	None	Inj. LMWH Tab. aspirin	Preterm labour	Good
35	6	Yes	Anti-SSA + ANA +	Hypertension, HSV +	T. dexa-methasone T. HCQS T. aspirin	Cholestatis of pregnancy Induction of labour	Poor
35	8	Yes	ANA +	Hypothyrodism	T. HCQS Tab. Aspirin T. levo-thyroxine	Encirclage done Preterm labour	Poor
32	12	Yes	LA + aCLA+	None	Inj. LMWH Tab Aspirin	None	Good
30	22	Yes	ANA +	Anaemia	Tab. Aspirin	None	Good
23	26	No	ANA +	None	Tab aspirin	Induction of labour	Good
27	29	No	ANA + U1SNRNP +	Autoimmune haemolytic anemia, Evans syndrome	T. prednisolone T. azathioprine T. HCQS	Preterm delivery	Good
31	8	Yes	ANA +	None	T. aspirin	Preterm delivery	Poor
31	13	Yes	ANA + U1SNRNP+	Hypothyroidism	T. prednisolone T. HCQS T. aspirin T. levo-thyroxine	Induction of labour	Good
25	8	Yes	ANA+	None	No medication	Abortion	Poor

DISCUSSION

The age range of our patients ranged from 23 to 35, with an average age of 29.9 years. The high mean age of presentation of patients with autoimmune disorders has been described in western literature and in similar settings by Kothari et al also.[3,4]

Fertility was poor in this group of patients studied, evidence by an average of married life to be around 7.5 years. Autoimmune oophoritis, drug induced ovarian dysfunction and disturbance of hypothalamo-pituitary axis due to chronic inflammatory state are all postulated as reasons for poor fertility outcomes in patients with autoimmune disorders.[5]

Though commonly used, NSAIDs should be avoided in early gestation due to a possible low risk of miscarriage and congenital malformations. HCQS, azathioprine, cyclosporine, tacrolimus and steroids are all considered to be safe in pregnancy.[6]

ANA positivity was seen in 8 patients. However, while in 5 patients it was the only autoimmune abnormality, there were other associated antibodies positive in the remaining three cases. Eight patients had a prior poor obstetric outcome (either abortion or still birth or neonatal death). It is now well established that the occurrence of miscarriage is much higher in patients with autoimmune disorders.[7,8]

Surprisingly, associated medical disorders were not common. Two patients had hypothyroidism and one patient had hypertension. These two medical disorders are reported to be more common in pregnancies with autoimmune disorders than without.[9] Three patients were on oral steroid medications throughout the pregnancy. Steroids have been reported to improve the rate of live births in some studies.[10] Four patients were on HCQS throughout the pregnancy. Though HCQS is given during pregnancy with SLE, there are suggestions that it may be used successfully in pregnancies with antiphospholipid antibody syndrome also.[11] Eight patients were on aspirin throughout the pregnancy. The use of low dose aspirin is well established in patients with autoimmune disorders, and is recommended by the EULAR (EUropean League Against Rheumatism).[12]

One patient had cholestasis of pregnancy. It is to be noted that there are upcoming hypotheses to state that cholestasis of pregnancy may be a risk factor for future autoimmune disorders.[13] One patient had a flare during pregnancy and required multiple medical interventions to

ensure maternal survival (case 7). Occurrence of flare is considered to be one of the most important predictors of poor maternal and neonatal outcomes.[14] Similar to what Tan et al had observed, this patient also presented as an autoimmune haemolytic anemia.[15]

Four patients had preterm delivery. Though we did not use any method to predict preterm delivery, Clowse et al have shown that apart from disease activity, biochemical markers like ferritin and uric acid can also predict premature birth.[7]

One of the patients had been detected to have fetal heart rate abnormality in the antenatal period. But on follow, it was found to have resolved and neonatal echocardiography showed no abnormality. However, it is now well established that congenital heart defects are higher among children born to women with autoimmune disorders.[16]

One patient had SLE + Evans syndrome (case 7), and though she had a difficult clinical course, there was maternal and neonatal survival. As recent as 2015, Nause et al had reported the first ever case of successful management of coexisting SLE and Evans syndrome. Our patient (case 7) is probably the second such case.[17]

Long term follow-up data of children born to autoimmune mothers should be maintained in developing countries like India, because it has now been recently demonstrated that a slightly increased risk of autism spectrum disorders exists.[18] Overall good neonatal outcome was seen in 60% of patients. Galappathy et al have reported an approximately 45% live birth rate in similar settings.[19]

Appropriate contraceptive methods had been advised to all patients to avoid unwanted pregnancy, especially to prevent any possible deterioration of maternal condition due to the medical disorder.

CONCLUSION

To conclude, autoimmune disorders in pregnancy when managed in a tertiary care centre with multidisciplinary approach can result in good obstetric and neonatal outcomes.

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