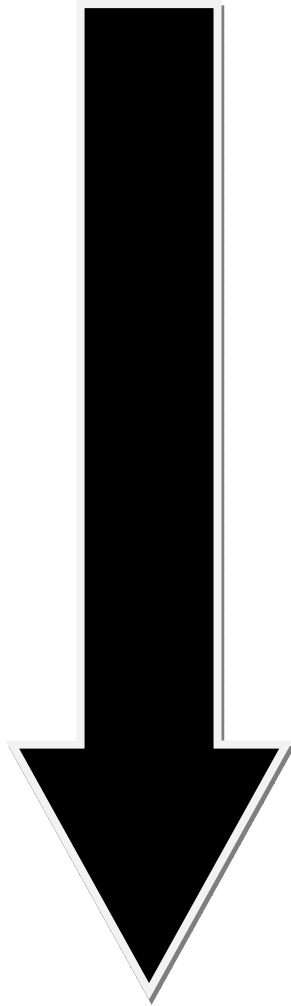


# **OBGY Department Publication 2020**



# Dysgerminoma with pregnancy and viable baby: A case report

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## Abstract

Dysgerminomas are the most common of primitive germ cell tumors of the ovary, accounting for 1-5% of all ovarian malignancies. The reproductive age group females are most commonly affected, thereby causing problems in conception and if pregnancy occurs, it leads to feto-maternal compromise. It is extremely rare to have a successful natural pregnancy, with viable child birth with a coexisting dysgerminoma, without any assisted reproductive interventions. We hereby report a case of successful spontaneous natural pregnancy in a G3P2L1D1, associated with dysgerminoma, with no feto-maternal compromise.

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## INTRODUCTION

Dysgerminomas are germ cell tumors of ovaries with excellent prognosis after surgery and/or chemotherapy. The challenge, however, lies in the fact that dysgerminomas, unlike other tumors of the ovary affect females in the reproductive age group, thus preservation of fertility even after treatment is uncertain; and if a concurrent pregnancy has occurred, then should it be allowed to progress? We present a case where the patient had no any prior intervention for the diagnosis and presented to us only when she had abdominal discomfort due to increased abdominal girth.

## CASE REPORT

A 22 years old female G3P2L1D1 with 8 months of amenorrhea referred from PHC, Sonpeth to our institute i/v/o large ovarian mass with abdominal fullness and decreased appetite since 15 days with difficulty in defecation since 4-5 days. Without any history of prior ANC check-up. There was no history of any menstrual irregularity or any contraceptive intake in the patient before the pregnancy. There was history of previous FTND 3 years back and history of 6 months IUD. Also there was no history of any major medical or surgical illness in the past or family history of any gynaecological and breast malignancy. No history of any chemotherapeutic drugs intake taken. Ultrasonographic examination revealed a pregnancy of 33wks 4days with e/o capsulated, mixed echogenic solid mass with no papillae or septi, of size 18.4cm \* 12.2cm arising from left ovary suggestive of? ovarian teratoma with right sided adnexal structure showing no pathology. On examination patient was afebrile, pallor ++, PR-94/min, BP- 110/74mmHg.on per abdominal examination overdistended abdomen with cephalic presentation with presenting part felt above the mass. FHS was heard regular 140/min with uterus relaxed. On per speculum examination cervical os not seen. On per vaginal examination cervical os could not be reached, posterior fornix is full of mass, POD was tense and tender. On per

rectal examination is rectum no other mass felt with rectum loaded with fecal matter. Patient was given enema and stool passed. In view of a viable foetus, emergency surgery was planned immediately after coverage of steroids due to severe pain in lower abdomen not related to uterine contraction. Laparotomy with Lower segment Caesarean Section was carried out. An enlarged left ovary with bosselated outer surface and intact capsule was noted. Ovarian mass of solid, fragile tissue, arising from

left ovary and occupying the whole pelvic cavity behind the uterus was present. No abnormality was observed in any other intra-abdominal organ and Right adnexal structures. A per-operative diagnosis of pregnancy with concurrent ovarian tumor was made. Left salpingo-ovariectomy was performed and a live male baby, appropriate for gestational age was delivered. The patient was referred to cancer institute for chemotherapy due to unavailability of the same in our institute.



Intraoperative picture showing left ovarian dysgerminoma

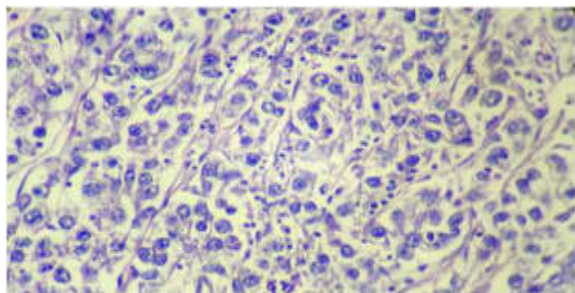
#### **PATHOLOGICAL FINDINGS**

**GROSS:** Received specimen in 4 pieces of ovary – first of size 19\*17\*8 cm, second of size 17\*9\*6 cm, third of size 7\*6\*3 cm and fourth of size 5\*2.5\*2.5 cm. External surface – capsulated, bosselated, congested blood vessels. On cut section – solid firm homogenous whitish coloured mass along with foci of hemorrhage and necrosis.



Grossly cut section shows solid, firm, homogenous, tan colored growth with foci of hemorrhage and necrosis

**MICROSCOPIC EXAMINATION:** Multiple sections studied revealed partly encapsulated tumor mass composed of well defined nest and cords of tumor cells separated by thin fibrous septa infiltrated by lymphocytes. Individual tumor cells are of uniform size having large nuclei and prominent nucleoli. Cells are having abundant finely granular to clear cytoplasm. Occasional multinucleated giant cells are also evident. Microscopically, the fallopian tube was normal. A final histopathological diagnosis of ovarian dysgerminoma (left side) was made.



Tissue section shows well defined nests of large uniform tumor cells with granular nuclear chromatin, prominent nucleoli and finely granular cytoplasm separated by fibrous strands containing lymphocytes, Hematoxylin and Eosin \* 40

## DISCUSSION

Ovarian tumors are broadly classified into three types based on their origin, epithelial, sex cord and germ cell tumors. While epithelial variety largely predominate, germ cell tumors (GCTs) are rare, comprising about 30% of all ovarian neoplasms and 3 % of all ovarian malignancies.<sup>1</sup> Ovarian Germ cell tumors, derived from the primordial germ cells, are further divided into subgroups based on the histological features. Mature teratoma being the commonest benign variety while dysgerminoma are the commonest malignant germ cell tumor.<sup>2</sup> Among the non-dysgerminoma group are yolk sac tumors, endodermal tumors, immature teratoma, embryonal carcinoma, choriocarcinoma and mixed germ cell tumors. The major challenge with dysgerminoma, the commonest malignant variety of germ cell tumor, is that they predominantly affect young women. About 75 % of dysgerminoma occur between the ages of 10 and 30 years and thus can affect the fertility or may be associated with pregnancy.<sup>1</sup> Lee *et al* reported the mean age of women in their study as 23.8 years (Range 4-63 years).<sup>3</sup> Several cases of pregnancies after treatment of dysgerminomas with various modalities including surgery and chemotherapy, have been reported previously.<sup>4,5</sup> Gershenson has reported that natural conception is possible in case of germ cell tumors of the ovary, a finding similar to our case.<sup>6</sup> Hirota *et al.* in their study reported the frequency of ovarian tumor associated with pregnancy ranges from 1:80 to 1:2200 deliveries.<sup>7</sup> But natural course of pregnancy in cases of dysgerminoma is extremely difficult, due to large sizes of the tumors, irregular menstruation, and collection of fluid as well as tubal adhesions. Ovarian tumors generally remain asymptomatic, until they are discovered due to their large size or related complications.<sup>8</sup> In the current case, dysgerminoma was diagnosed due to disproportionate enlargement of the abdomen because of large ovarian mass with pregnancy. The patient in this report deserves

attention as she conceived naturally, without any assisted reproductive technique and spontaneous delivery was possible with a coexisting dysgerminoma. Quirk and Natarajan have reported that approximately 75% of women with a dysgerminoma present with clinical stage Ia disease.<sup>9</sup> Dysgerminoma disease staged Ia (ie, confined within the capsule of only one ovary) is best treated with simple unilateral salpingo-oophorectomy and residual microscopic disease is extinguished readily with chemotherapy, to which these cells are highly responsive.<sup>10</sup> The best outcome for both mother and child depends on early diagnosis and excision of the ovarian lesion while it is still intact. The pathologic type and extent of ovarian carcinoma seem to be the most important determining factors in the maternal prognosis. Several authors have stated that once the existence of ovarian malignancy is suspected, immediate laparotomy is indicated regardless of the stage of gestation.<sup>11-13</sup> But Jubb, supports a more conservative approach in younger pregnant patients, especially if the ovarian lesion is intact or is of the pseudomucinous type.<sup>14</sup> There still remain unsolved problems concerning conservative management before and after termination for early-stage ovarian malignancy associated with pregnancy. When we encounter FIGO stage-Ib or higher ovarian malignancies in the second trimester and the patient strongly wishes to continue with the pregnancy, very serious problems arise as to whether conservative surgery and chemotherapy should be performed in the gravid woman or not. Antineoplastic agents can be mutagenic or teratogenic, or cause fetal growth retardation or fetal death when used in the first trimester.<sup>15</sup> However, Kim and Park, have documented the use of chemotherapeutic agents during the second trimester and delivery of a normal infant.<sup>16</sup> Patterson *et al.* in their review of the close surveillance policy for stage I female germ cell tumors of the ovary, stated that five-year survival rate for Stage Ia dysgerminomas is over 95%.<sup>17</sup> Our patient was advised close follow up in terms of regular pelvic examination and abdominal CT scan as there was no evidence of metastasis and complete resection of tumor mass was possible in our case.

## CONCLUSION

The long-term outcome of patients with pure ovarian dysgerminoma is excellent. Patients can be treated with fertility-sparing surgery and can expect good reproductive outcomes. A dysgerminoma confined to a single ovary, with ascites, although large may not metastasize or seed the peritoneal cavity/fluid or other pelvic/abdominal organs and a natural course of pregnancy with viable child birth may still be possible.

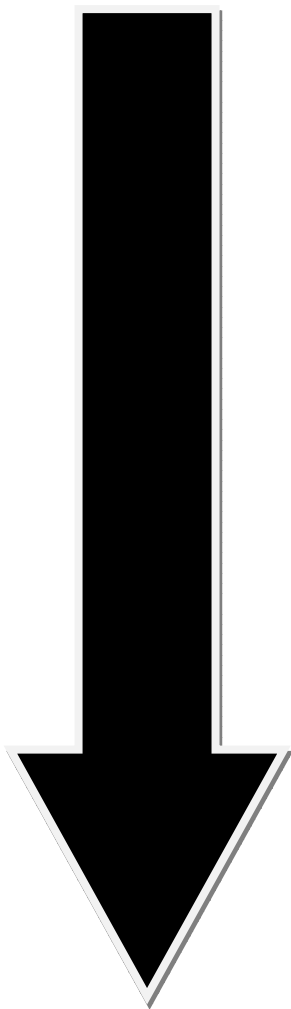


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# **Surgery Department Publication 2019**



# Clinico-morphological pattern of breast lump in tertiary care hospital

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## Abstract

**Background:** For developing countries, where the facility for detecting cancer at an early stage is not possible, symptomatic findings can be used as an indication for early diagnosis which could prevent the women from late stage presentation of disease. **Aim:** To describe some of the clinico-morphological features of the breast lump cases seen at a tertiary level hospital. **Material and Methods:** In clinically selected 100 cases, triple approach including clinical examination coupled with ultrasonographic examination (USG) and mammography was also carried out. USG was carried out to assess the extent of the axillary lymph nodes more precisely. Diagnosis was confirmed by core-cut biopsy, tru-cut biopsy and frozen section biopsy. **Results:** Out of 52 clinically diagnosed as carcinomas 50 were proved correct on histopathologically while 86 fibroadenomas diagnosed on clinical examination 2 turned out to be malignant on histopathology. **Conclusion:** Patients of breast cancer are coming to a tertiary level hospital very late, mostly with clinical features of advanced disease. Understanding its clinical and morphological features holds a great promise for early detection and prevention of this cancer.

**Key Words:** Breast lump, fibroadenoma, malignancy, clinical diagnosis, histopathology.

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## INTRODUCTION

Breast cancer is the most common malignancy in world and second most common in India after cancer cervix. Among humans it is widely distributed throughout the world. It is now considered as systemic disease rather than loco-regional disease.<sup>1</sup> Early detection of breast cancer through organized screening in unselected women with an average risk in target populations has been impressive in reducing the mortality from the disease. Moreover, awareness regarding the diagnosis of early signs and symptoms in symptomatic population with

access to high quality treatment service is another way of preventing the fatal outcome. Detection refers to the recognition of any sign of symptom of disease. Technique used for the detection include history, physical examination, mammography, thermography, fine needle aspiration cytology and biopsy. By contrast there is only one method of making a definitive diagnosis – Histological examination of a tissue specimen.<sup>2</sup> For developing countries, where the facility for detecting cancer at an early stage is not possible, symptomatic findings can be used as an indication for early diagnosis which could prevent the women from late stage presentation of disease. We proposed a study to examine the clinical validity of the symptoms as well as the associated between symptoms and tumors characteristics. The ever increasing incidence of malignancy in general and breast in particular, associated with increased consciousness among females for any abnormal feel in the breast, and lack of much data about breast lumps from different parts of our country, have prompted us to study the clinico-morphological pattern of breast lump cases.



## MATERIAL AND METHODS

This prospective study of the clinical evaluation of breast lumps was conducted at Tertiary Health Care Centre over a period of two years.

### Inclusion criteria

- Any patient attending the surgical department directly or referred with a definite breast lump.

### Exclusion criteria

- Pre-pubertal females with breast buds being perceived as lumps.

In clinically selected 100 cases, triple approach including clinical examination coupled with ultrasonographic examination (USG) and mammography was also carried out. USG was carried out to assess the extent of the axillary lymph nodes more precisely. Axillary lymph node examination was done clinically as well as by ultrasound. Most of the patients of breast cancer that we receive are locally advanced cancers and have palpable lymph nodes. In case of male breast, past history of hepatitis, malnutrition, renal failure, chronic chest diseases and Hansen's disease along with drugs

history of taking estrogen, tranquilisers, diuretics and steroids was done. Examination of genitalia (testis) was also done. Diagnosis was confirmed by core-cut biopsy, tru-cut biopsy and frozen section biopsy.

## RESULTS

One hundred cases suffering from various types of breast lumps have been studied, and a large majority 52 were clinically suspected to be suffering from cancer; while 96 were neoplastic and 52 were non-neoplastic. In neoplastic (benign), fibroadenoma were suspected in 86 cases, duct papilloma 2 cases and gynecomastia 8 cases; while in non-neoplastic group, inflammatory lumps were 46 cases and fibroadenosis in 6 cases. Majority of benign cases were found to be in the age-group of below 40 years, while malignant lumps were found to be in age group above 40 yrs. Majority of the inflammatory cases (abscess) were found to have early onset of symptoms with acute history of less than 2 wks while non-inflammatory cases like carcinoma and fibroadenomas have history of more than 2 wks.

Table 1: Physical findings in different breast lumps histopathologically proved

| Clinical findings | Carcinoma | Fibro adenoma | Fibro adenosis | Inflammatory | Duct papilloma | Gynae comstia |
|-------------------|-----------|---------------|----------------|--------------|----------------|---------------|
| Breast            |           |               |                |              |                |               |
| Right             | 22        | 44            | 04             | 24           | 01             | 04            |
| Left              | 28        | 40            | 02             | 22           | 01             | 04            |
| Bilateral         | 02        | 02            | --             | --           | --             | --            |
| Nipple position   |           |               |                |              |                |               |
| Normal            | 04        | 82            | 06             | 22           | --             | 08            |
| Destruction       | 02        | --            | --             | 02           | 02             | --            |
| Retraction        | 26        | 03            | --             | 02           | --             | --            |
| Displacement      | 12        | 01            | --             | --           | --             | --            |
| Discolouration    | --        | --            | --             | --           | --             | --            |
| Deviation         | 06        | --            | --             | 20           | --             | --            |
| Discharge         | 02        | --            | --             | --           | --             | --            |
| Areola            |           |               |                |              |                |               |
| Normal            | 40        | 80            | 06             | 44           | 02             | 08            |
| Crack             | 02        | 02            | --             | --           | --             | --            |
| Fissure           | 02        | --            | --             | --           | --             | --            |
| Ulcer             | 04        | --            | --             | 01           | --             | --            |
| Eczema            | --        | 04            | --             | --           | --             | --            |
| Discharge         | 04        | --            | --             | 01           | --             | --            |
| Skin over breast  |           |               |                |              |                |               |
| Normal            | 06        | 84            | 06             | 05           | 02             | 06            |
| Redness           | 08        | 02            | --             | 40           | --             | 02            |
| Dimpling          | 04        | --            | --             | --           | --             | --            |
| Retraction        | 03        | --            | --             | --           | --             | --            |
| Puckering         | 03        | --            | --             | --           | --             | --            |
| Peau'd orange     | 18        | --            | --             | --           | --             | --            |
| Tethering         | 04        | --            | --             | --           | --             | --            |
| Fungation         | 02        | --            | --             | --           | --             | --            |
| Ulceration        | 04        | --            | --             | --           | --             | --            |
| Breast            |           |               |                |              |                |               |
| Normal            | 20        | 80            | 06             | 06           | 02             | 08            |



|                   |    |    |    |    |    |    |
|-------------------|----|----|----|----|----|----|
| Enlarged          | 18 | 06 | -- | 40 | -- | -- |
| Retracted         | 14 | -- | -- | -- | -- | -- |
| Quadrant involved |    |    |    |    |    |    |
| Upper outer       | 20 | 27 | 02 | 08 | -- | 05 |
| Upper inner       | 06 | 18 | 01 | 05 | -- | 02 |
| Lower inner       | 08 | 18 | 01 | 06 | -- | 01 |
| Lower outer       | 10 | 19 | -- | 20 | -- | -- |
| Central           | 04 | 04 | -- | -- | 02 | -- |
| Tail of spence    | 02 | -- | -- | -- | -- | -- |
| All quadrants     | 02 | -- | 02 | 02 | -- | -- |

Table 2: Morphological characteristics of different breast lumps

| Lump characters            | Carcinoma | Fibro adenoma | Fibro adenosis | Inflammatory | Duct papilloma | Gynae comstia |
|----------------------------|-----------|---------------|----------------|--------------|----------------|---------------|
| Size                       |           |               |                |              |                |               |
| 1x1 cm and below           | 06        | 19            | --             | 08           | 01             | --            |
| 2x2 cm                     | 12        | 19            | --             | 06           | 01             | --            |
| 3x3 cm                     | 18        | 25            | 03             | 16           | --             | 04            |
| 4x4 cm and above           | 16        | 23            | 03             | 16           | --             | 04            |
| Shape                      |           |               |                |              |                |               |
| Rounded                    | 18        | 48            | --             | 42           | --             | 04            |
| Discoid                    | 16        | 21            | 04             | --           | --             | 03            |
| Irregular                  | 18        | 17            | 02             | 04           | 02             | 01            |
| Margins                    |           |               |                |              |                |               |
| Well organized             | 10        | 84            | --             | 24           | --             | 08            |
| Diffuse                    | 42        | 02            | 06             | 22           | 02             | --            |
| Tenderness                 |           |               |                |              |                |               |
| Present                    | 16        | 50            | 05             | 34           | --             | 08            |
| Absent                     | 36        | 36            | 01             | 12           | 02             | --            |
| Consistency                |           |               |                |              |                |               |
| Soft                       | 04        | 08            | 04             | 12           | --             | --            |
| Firm                       | 20        | 56            | 02             | 34           | 02             | 08            |
| Hard                       | 28        | 22            | --             | --           | --             | --            |
| Fixity of lump             |           |               |                |              |                |               |
| Mobile                     | 06        | 74            | 06             | 14           | --             | 08            |
| Breast alone               | 08        | 12            | --             | 32           | --             | --            |
| Breast and skin            | 22        | --            | --             | --           | 02             | --            |
| Breast and skin and muscle | 14        | --            | --             | --           | --             | --            |
| Chest wall                 | 02        | --            | --             | --           | --             | --            |

All the patients came with lump as primary complaints except in cases of duct papilloma, in which patient came with nipple discharge as a primary complaint. The second most common feature was pain seen in remaining patients while patients of breast carcinomas had noticed retraction of nipple.

Table 3: Common presenting symptoms in different lumps histopathologically proved

| Diagnosis      | Lump | Pain | Nipple Retraction | Skin Involvement | Nipple discharge |
|----------------|------|------|-------------------|------------------|------------------|
| Carcinoma      | 42   | 20   | 24                | 16               | 2                |
| Fibroadenoma   | 66   | 12   | -                 | -                | -                |
| Fibroadenosis  | 4    | 4    | -                 | -                | -                |
| Inflammatory   | 6    | 34   | -                 | -                | -                |
| Duct Papilloma | 2    | 2    | -                 | -                | 2                |
| Male breast    |      |      |                   |                  |                  |
| Gynaecomastia  | 8    | 6    | -                 | 2                | -                |
| Carcinoma      | 2    | 2    | 1                 | 1                | -                |

All the patients diagnosed as carcinoma are having metastasis in axillary lymph node; in only 2 cases were having the distant metastasis. In fibroadenoma, only two cases were having the lymph node involvement while 26 cases were lymph node involvement in inflammatory group.

Table 4: Clinically diagnosed distribution of cases studied

| Clinical diagnosis    | No. of cases | Percentage |
|-----------------------|--------------|------------|
| Non neoplastic (n=52) |              |            |
| Inflammatory          | 46           | 88.4%      |
| Fibroadenosis         | 06           | 11.6%      |
| Neoplastic (n=96)     |              |            |
| Fibroadenoma          | 86           | 89.5%      |
| Duct Papilloma        | 02           | 2.1%       |
| Gynaecomastia         | 08           | 8.3%       |
| Malignant (n=52)      |              |            |
| Female                | 50           | 96.1%      |
| Male                  | 02           | 3.9%       |

In malignant group, male breast lumps 2 were clinically suspected of cancer. All these lumps were subjected to biopsy for histopathological confirmations of diagnosis. Out of 52 clinically diagnosed as carcinomas 50 were proved correct on histopathologically while 86 fibroadenomas diagnosed on clinical examination 2 turned out to be malignant on histopathology.

## DISCUSSION

The present study is comprised of 200 cases of breast lump that were studied prospectively at tertiary health care centre situated in rural area. Carcinoma of the breast occurs mainly in the 4th and 5th decade. The disease occurs generally a decade earlier in Indians as compared to white population. Breast carcinoma is rare in males. We found 2 cases of carcinoma in males and 8 cases of gynaecomastia. Out of 52 cases of carcinoma 28 were having left breast involvement, 22 were having right breast involvement and 2 cases were having bilateral breast involvement. In the study by Nuruzzaman HSM, left breast was affected in 67% cases, 28% in the right breast and the rest had bilateral involvement.<sup>3</sup> Classically there is a left sided predominance.<sup>2</sup> The side affection possibly does not have much effect so far the treatment and prognosis are concerned. In our study, retracted nipple was most common finding in carcinoma breast whereas 40 cases of carcinoma breast were having normal areola. Most common finding was a peau'd orange in cases of breast skin involvement, 68% among all cases of breast lump were having normal breast size. In Nuruzzaman HSM study, 71.66% cases presented with painless lump, 28.33% with painful lump, 20% with ulceration, 8.33% with nipple discharge and 40% with nipple retraction.<sup>3</sup> Haagensen study shows that 75% to 80% of women suffering from carcinoma breast presents with a lump in the breast.<sup>4</sup> Nair *et al* have shown that lump in the breast was the presenting symptom in 88%, ulceration 8% and nipple retraction in 8% cases.<sup>5</sup> Another study was carried out by Vinod Raina *et al* in India, where 96% of the patient in premenopausal women presented with breast lump, 15.8% with pain and 4.4% came with nipple discharge.<sup>6</sup> Upper outer quadrant was the most common site of involvement in cases of carcinoma. In a study by Nuruzzaman HSM, the most frequent site involved was upper outer quadrant (in 54%

cases). In 15% cases it was central, 13% in Lower outer quadrant, 10% in lower inner, 5% in upper inner quadrant and overlapping lesions were in 3% cases.<sup>3</sup> A study carried out in Kerala, India has shown 31% of the growth in upper-outer quadrant, 8% in lower-outer quadrant, 11% in the upper-inner and 29% affected the whole breast.<sup>5</sup> In present study, 34 cases presented when their lump size was more than 3 centimetre. 42 cases out of 52 were having diffuse margins as compared to 10 cases with well-defined margins. 28 cases were having hard palpable mass, 20 were having firm and 4 cases were having soft palpable mass among all the cases of carcinoma breast. Firm mobile mass was the most common finding on examination in cases of fibroadenomas. 22 cases of carcinoma breast were having skin involvement and only 2 cases had chest wall involvement suggesting advanced disease. A study carried out in USA by Swanson *et al* showed that 65.5% of the younger women presented with a lump more than 2 cm in diameter.<sup>7</sup> Another study carried out by Raina V *et al* showed 74.1% patients presented with tumor size more than 2 cm but less than 5 cm and 12.3% with tumor size more than 5 cm.<sup>6</sup> This shows that our patients present quiet late and with a higher stage of disease to a tertiary center. Palpable lump with nipple retraction was the most common finding on clinical examination in cases of carcinoma breast. Axillary group of lymph nodes were the most common lymph nodes involved in cases of carcinoma (44 cases). Only 6 cases were having cervical lymph node involvement, and 1 each were having other axilla involvement and distant metastasis. In the series by Nuruzzaman HSM, among the 60 patients, 52 patients had clinically palpable lymph nodes (86.66%). Among them 48% had one group of lymph node involved, 23% had two groups and 29% had more than two groups involved. The rest (13.33%) had no lymph node palpable clinically.<sup>3</sup> Out of 200 cases 52 were suspected as



carcinomas and 86 were suspected as fibroadenomas. After FNAC 2 cases among suspected carcinomas were reported as fibroadenomas whereas 2 cases among suspected fibroadenomas were reported as carcinomas.

## CONCLUSION

Patients of breast cancer are coming to a tertiary level hospital very late, mostly with clinical features of advanced disease. Early detection of carcinoma can avoid distant metastasis and advanced breast carcinoma. Only 1 patient in our study had distant metastasis and 1 patient had spread to other axilla. On clinical examination correct diagnosis was found in 96.2% of malignancy and 98.6% of benign lesions.

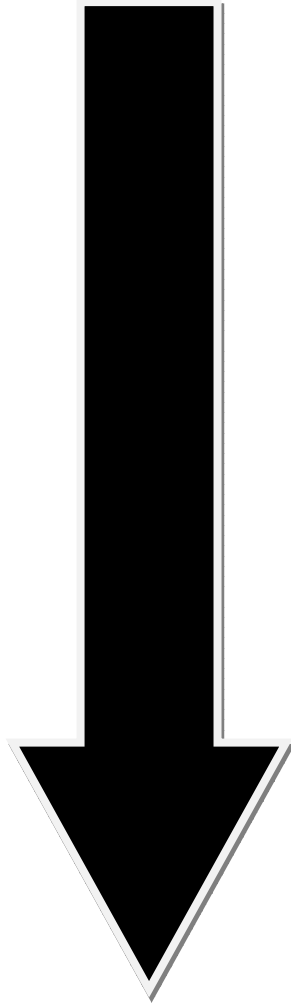
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# **Anatomy Department Publication 2019**





## HISTOGENESIS OF HUMAN FOETAL THYMUS

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### ABSTRACT

**Introduction:** The thymus is a primary lymphoid organ. It is a bilobed structure divided into lobules by the connective tissue septa. Each lobule consists of a cortex and medulla. Most of the studies regarding early foetal histology of this organ are animal based. The present study has been undertaken to highlight some features regarding histogenesis of human foetal thymus.

**Materials and Methods:** In the present study, 30 normal human stillborn/aborted fetuses were studied. The obtained fetuses were fixed in 10% formalin. After proper fixation they were subjected to dissection. The obtained specimens were processed by standard paraffin block making procedure. Sections were taken and stained with haematoxylin & eosin. The stained sections were examined under light microscopy using 10x and 40x optical magnifications and photographs taken.


**Results:** At 12<sup>th</sup> week, capsule was thin and cortico-medullary differentiation not much prominent. Epithelial cells and lymphocytes were present. Hassall's corpuscles were very small and immature. Distinct lobulation was seen at 18<sup>th</sup> week with well differentiated cortex and medulla. The gland became more distinct from 21<sup>st</sup> week onwards with increased number of Hassall's corpuscles of various types. 29 week onwards the thymus gland revealed an adult histological picture.

**Conclusion:** All structural changes viz cortico-medullary differentiation, lobulation and maturity of Hassall's corpuscles occurred within the first 18 weeks of gestation.

**KEY WORDS:** Thymus, Hassall's corpuscle.

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### INTRODUCTION

The thymus is a primary central lymphoid organ and a key regulator of the immune system, and is responsible for cellular immunity of the body. It is a bilobed structure divided into lobules by the connective tissue septa. Each lobule consists of cortex and medulla [1].

Thymus consists of two pyramidal lobes. It is located in the mediastinum behind the sternum

and in front of the pericardium and great vessels of the heart in the adult. The primordia of thymus develop in the region of superior neck in early fetal life and reach final destination in the mediastinum by progressive descent [2].

The details of microscopic & morphometric development of the thymus are not studied to great extent in the human fetuses and most of our knowledge regarding early fetal histology of this

organ is based on the studies in different animals. Thus the findings of different workers are found to be not consistent and are contrasting in most of the cases. The present study has been undertaken to highlight some important points in histogenesis of normal human foetal thymus gland.

## MATERIALS AND METHODS

Histological study of Thymus gland in human foetuses of various gestational ages was carried out in the department of Anatomy in collaboration with department of Obstetrics and Gynaecology S.R.T.R Medical college Ambajogai, Maharashtra, India.

In the present study 30 normal foetuses were obtained from the department of Obstetrics & Gynaecology S.R.T.R Medical college and hospital Ambajogai with the permission of Professor & Head of department. These fetuses included the spontaneous abortus and still born. For the above purpose the approval was also taken from the Local Ethical Research Committee. A full anatomical examination was performed in all specimens to document normal anatomical development. A standard proforma was designed and used to maintain a protocol in selecting only the normal fetuses. Twin foetuses and foetuses with gross anomalies were omitted from the study. Foetuses were collected within 3-4 hours immediately after the delivery to avoid post-mortem changes.

The obtained foetuses were fixed in 10% formalin. After proper fixation they were subjected to dissection. All the specimens were processed by standard paraffin block making procedure. The sections were taken by rotatory microtome and stained with haematoxylin & eosin. The stained sections were examined by using light microscope under 10x and 40x optical magnifications, photographs were taken.

Foetuses were arranged into three gestational age groups as follow:

**Group I-** 12-20 weeks,

**Group II-** 21-28 weeks,

**Group III-** 29-38 weeks.

## RESULTS

**Group-I (12-20 weeks):** At 12<sup>th</sup> week gland was seen to be composed of delicate capsule.

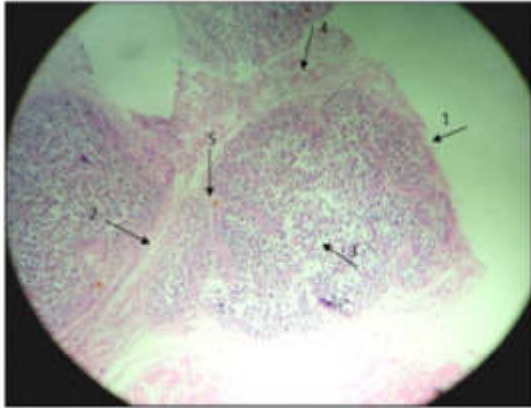
Connective tissue septa (trabeculae) extend from capsule into the parenchyma. Small immature connective tissue septa arising from these trabeculae extended partially into the lobule were seen (Fig. 1). Cortico-medullary differentiation was not that much prominent, lymphocytes present at this stage. Lymphocytes can be differentiated by large dark blue staining nucleus with faint eosinophilic cytoplasm. Immature blood vessels were seen in the connective tissue of capsule & trabeculae. Epithelial cells were seen at this stage. The cells can be differentiated by the pale staining nucleus with eosinophilic cytoplasm, the cells shows cytoplasmic extensions forming network. Hassall's corpuscles were seen at this stage. These were very small & immature (Fig. 2).

At 14<sup>th</sup> week the connective tissue septa were wider & Lobulation is still continued at this stage. Corticomedullary differentiation was still continued. Epithelial cells were irregular in shape with many processes extending among the lymphocytes. Few small Hassall's corpuscles were visible in the medulla as concentrically arranged epithelial cells with central eosinophilic mass.

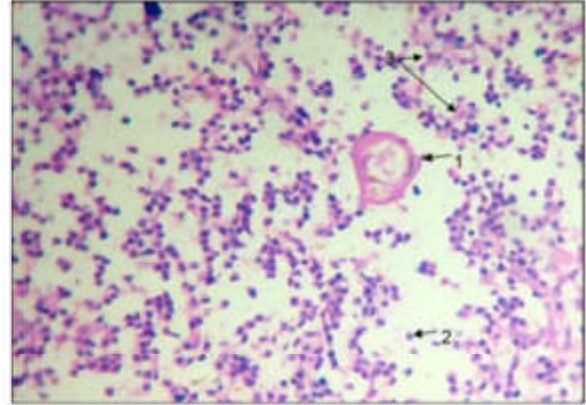
At 18<sup>th</sup> week Distinct lobulation was seen. The thicker connective tissue septa penetrate deeper into the substance of gland. Lobules increased in size, with increase in lobulation. Corticomedullary differentiation was complete at this stage. At the periphery of lobules numerous and densely packed lymphocytes forming darkly stained cortex were seen. At the centre lymphocytes were fewer and forming lightly stained medulla. Medulla continuous with one lobule to another (Fig. 3). Larger blood vessels were seen in the surrounding connective tissue capsule, trabeculae & parenchyma of thymus. Many Hassall's Corpuscle seen at various stages of development. Juvenile type composed of one or two hypertrophic reticuloepithelial cells. Premature type composed of small groups of hypertrophic cells showing early processes of keratinization, but without a flattened aspect, or a tendency to concentric disposition. In mature stage, the reticulo-epithelial cells appeared flattened and disposed concentrically around keratin and a mix of degenerated lymphocytes and macrophages, with or without empty space. Some Hassall's corpuscle of juvenile type, some



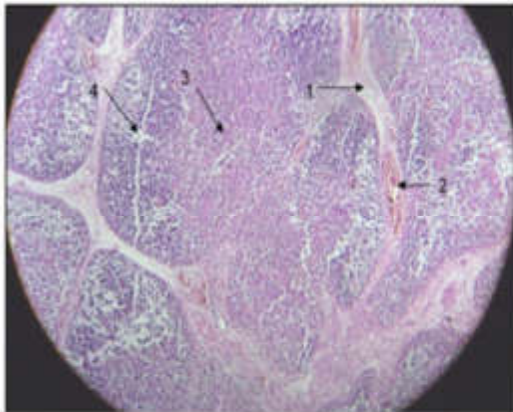
**Fig. 1:** 12 week 10x 1) Capsule, 2) Connective tissue septa, 3) Lobule, 4) Blood Vessel, 5) Immature Connective tissue Septa.



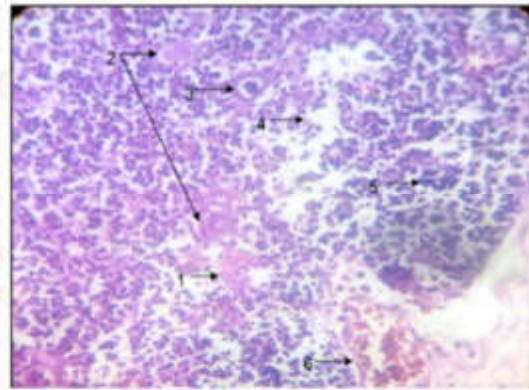
**Fig. 2:** 12 week 40x 1) Hassall's Corpuscle, 2) Lymphocytes, 3) Epithelial cells.



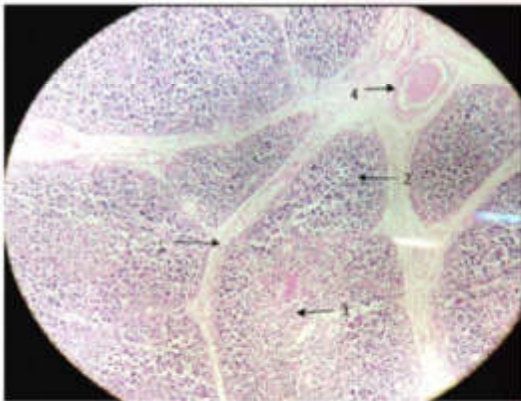
**Fig. 3:** 18 week 10x 1) Connective tissue septa, 2) Blood Vessel, 3) Medulla, 4) Cortex.



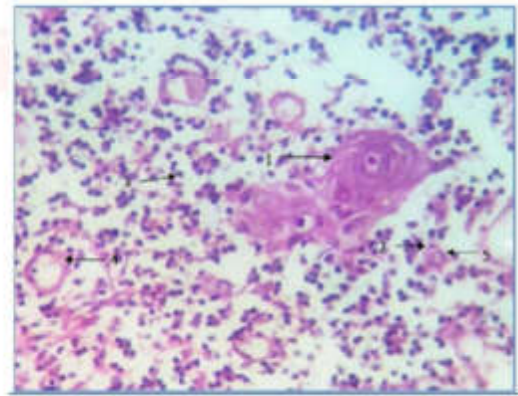
**Fig. 4:** 18 week 40x 1) Juvenile Hassall's Corpuscle, 2) Immat Corpuscle, 3) Mature Hassall's Corpuscle, 4) Epithelial Cell, 5) Lymphocytes, 6) Blood Vessel



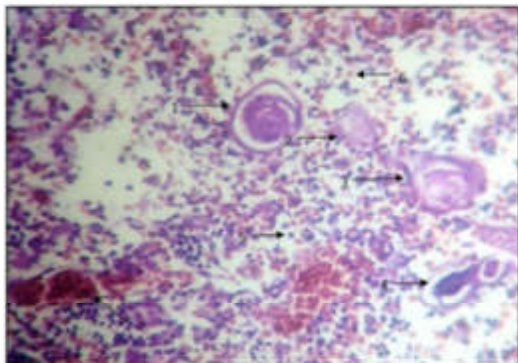
**Fig. 5:** 26 week 10x 1) Connective tissue septa, 2) Cortex, 3) Medulla, 4) Blood Vessel.



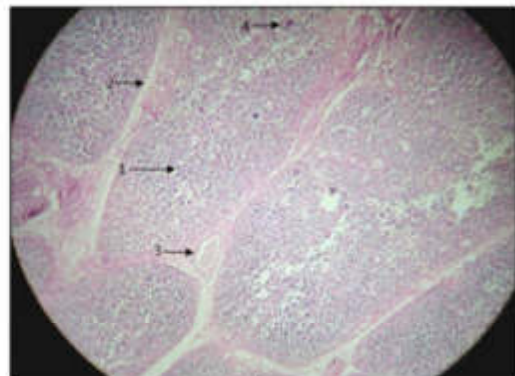
**Fig. 6:** 26 week 40x 1) Advanced Hassall Corpuscle, 2) Epithelial Cell, 3) Lymphocyte, 4) Blood Vessel, 5) Juvenile Hassall Corpuscle.



**Fig. 7:** 28 week 40x 1) Advanced Hassall Corpuscle, 2) Juvenile Hassall Corpuscle, 3) Immature Hassall Corpuscle, 4) Advanced Hassall Corpuscle, 5) Lymphocyte, 6) Epithelial Cell, 7) Blood Vessel.

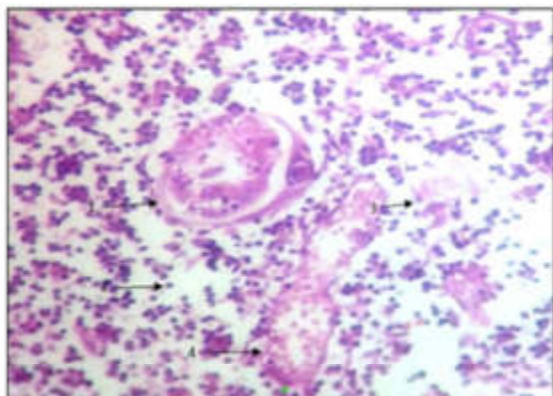


**Fig. 8:** 32 week 10x 1) Lobule, 2) Connective tissue septa, 3) Blood Vessel, 4) Hassall's corpuscle.

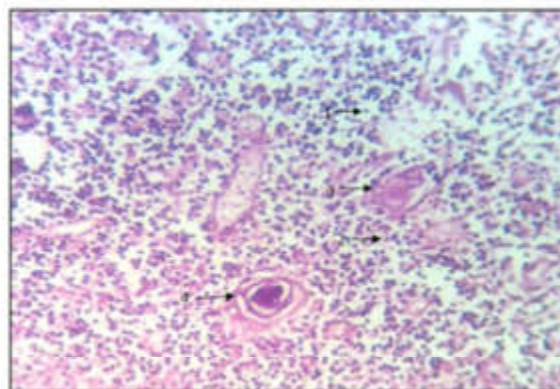




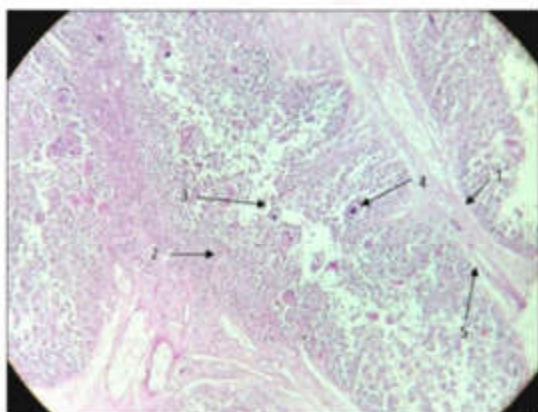
**Fig. 9:** 36 week 40x 1) Lymphocyte, 2) Epithelial Cell, 3) Immature Hassall Corpuscle, 4) Advanced Hassall Corpuscle.



**Fig. 10:** 32 week 40x 1) Advanced Hassall Corpuscle, 2) Lymphocyte, 3) Epithelial Cell, 4) Blood Vessel.



**Fig. 11:** 38 week 10x 1) Connective tissue septa, 2) Cortex, 3) Medulla, 4) Hassall Corpuscle, 5) Blood Vessel.



**Fig. 12:** 38 week 40x 1) Advanced Hassall Corpuscle, 2) Mature Hassall Corpuscle, 3) Lymphocyte, 4) Epithelial Cell.



of premature type and mature type were seen (Fig. 4).

The gland appears to be fully differentiated at this stage.

**GROUP-2 (21-28 weeks):** Connective tissue of capsule covering the gland became very much distinct at this stage. Septa (trabeculae) became more extensive at this stage. Connective tissue septa (trabeculae) also became thin and fine. Cortex and medulla became very much distinct at this stage. There was dense population of lymphocytes in the cortex and fewer in the medulla. Clear demarcation between cortex and medulla was seen (Fig. 5). Larger blood vessels were seen in the connective tissue septa. Also smaller blood vessels were seen at corticomедullary junction. The observed blood vessels were of larger size than that of previous group. Also observed blood vessels were more numerous & extensive. Epithelial cells were irregular in shape with many processes forming network.

Numbers of Hassall's corpuscle were more than that of previous stage. Various types of Hassall's corpuscle were seen such as Juvenile, prema-

ture, mature and Advanced. Advanced type of Hassall's corpuscle consists of varying degrees of deposition of materials at their center or periphery, whereas others HC with a distorted shape seemed to try and fuse with other nearby HC. (Raica et al) [3] (Fig. 6, 7)

**GROUP-3 (29-38 weeks):** The gland during this stage had an internal architecture seen in adult, with mature histological picture. Lobules of larger size were observed. The trabecular framework became more and more distinct at this stage. Corticomедullary junction was distinctly observed at this stage. Mature and larger blood vessels were seen at this stage. Blood vessels were increased in number with mature vascular framework (Fig. 8, 11). Numerous Hassall's corpuscles were present in the medulla. Various types such as Juvenile, Premature, Mature and Advanced were seen. Advanced type of Hassall's corpuscle were more numerous at this stage. They showed a graded series of increasing maturity (Fig. 9, 10, 12).

## DISCUSSION

**Lobulations:** In the present study lobulation was present at 12th week, although lobulation still



continued at 12th week stage. Distinct lobulation present at the 18th week stage. Ghali et al [4] observed the lobulation at 10th week. Harr [5] reported the lobulation at 12th week. Ajita et al [1] found that formation of lobules started at 9th week and distinct lobules were seen at 12th week. Varga et al [6] reported noticeably wide interlobular septa at 14-16 week, Krishnamurthy JV et al [7] observed it at 16 week whereas present study observed at 14-18 week.

**Cortex and Medulla:** In the present study the differentiation of the cortex and the medulla was noticed during 12th week but was not much prominent and it became started to distinguish from 14th week stage onwards which was completed at 18th week.

Varga et al [6] was reported it at 13th week. At 14th week by Harr [5] and Lobach and Haynes. [8] Between 12th and 14th weeks by Von Gaudecker. [9] Ajita et al [1] reported that differentiation of cortex and medulla started at 9th week and it become more distinct at 12th to 14th week.

**Blood Vessels:** In the present study blood vessels were noticed at 12th week, Since the present study examined foetuses from 12th week onwards, it could not be ascertained when blood vessels starts to appear before 12th week. They became larger, mature and more numerous in second group onwards.

Ghali et al [4] reported that thymus was vascular at 11th week of gestation. Harr [5] and Hamilton and Mossman [10] reported that extrathymic blood vessels associated with connective tissue fibers and mesenchymal cells surrounding the thymus were present at 9th week. Williams et al [11] mentioned of the developing erythroblastic cell by 10th week old thymic tissue.

**Epithelial Cells:** As the present study carried out from 12th week onward only, the epithelial cells were seen from this week onwards. Since foetuses prior to 12th week were not examined in the present study, it could not be ascertained whether epithelial cells were present at the earlier stages.

Williams et al [11], Hamilton and Mossman [10] described the presence of epithelial cells from 8th week. Hayward [12] reported that the

epithelial component of the thymus was recognizable at 10th week.

**Hassall's Corpuscles:** In the present study the Hassall's corpuscle was first observed at 12th week of gestation. Hassall's Corpuscles increased in number and size during 18th to 24th week. These Hassall's corpuscles had variable sizes, ranging from very small to very large whereas smallest size was represented by early age foetuses. The shape of Hassall's corpuscles varied significantly. Various types like juvenile, immature, mature, advanced observed irrespective of gestational age, with advanced type more significantly in foetuses above 28 week of gestational age.

This polymorphic behavior of Hassall's Corpuscle observed in present study coincides with the findings of Asghar A. et al. [13].

Fawcett, et al. [14] was reported appearance of Hassall's Corpuscles as early as 8th week of gestation, From 9th week Gilhus et al [15], Ghali et al [4] was reported it at 11th week, At 12th week by Sawant [16], Ajita et al [1] reported the presence of Hassall's Corpuscles was observed from 15th week of gestation. Krishnamurthy JV et al [2] observed that Hassall's Corpuscles increased in number and size during 17th to 24th week.

**Completion of Differentiation:** In the present study, all significant structural changes occur in thymus within 18th week of gestation; these findings are in accordance with Sawant SP [16] who reported that differentiation was completed at 18th week. Ajita et al [1] mentioned that thymus appeared fully differentiated at 17th week.

## CONCLUSION

The present study concludes that at 12th week, lobulation was incomplete. Distinct lobulation was seen from 18th week onwards. The cortico-medullary differentiation was started to distinguish from 14th and completed at 18th week. The 12th week foetus showed presense of immature, small blood vessels in the connective tissue of capsule & septa. In the II<sup>nd</sup> group onwards the blood vessels became larger, mature, and numerous. Epithelial cells were first observed at 12th week of gestation. They showed processes forming network.

The Hassall's corpuscle was first observed at 12th week of gestation. Hassall's Corpuscles increased in number and size during 18th to 24th week of gestation. Advanced types of Hassall's corpuscles were more significantly observed in fetuses from 28 week onwards. Polymorphic behavior was observed. All structural changes were occurred in thymus within 18 week of gestation.

**Conflicts of Interests: None**

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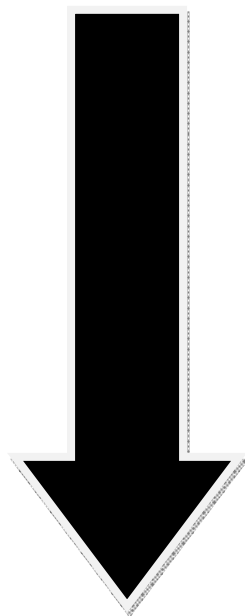
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# **PSM Department Publication 2019**



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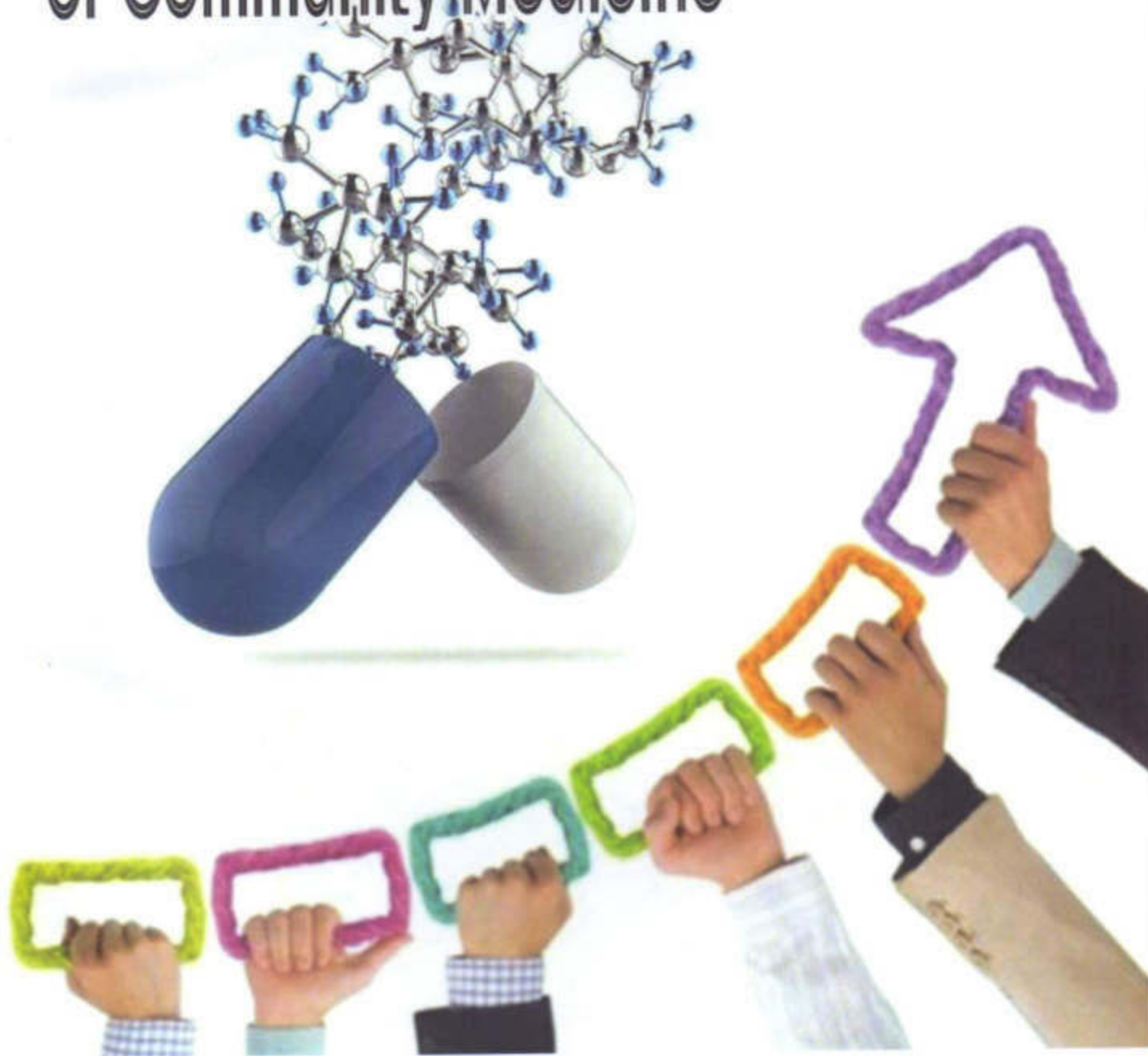
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# Medpulse International Journal of Community Medicine



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# Assessment of depression in a rural population of productive age group using patient health questionnaire

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## Abstract

**Background:** Health is pivotal for the growth, development, and productivity of a society and is vital for a happy and healthy life. It has been stated that No Health without mental health. Depression is a disorder of major public health importance, in terms of its prevalence, suffering, dysfunction, morbidity and economic burden. It has been estimated that the burden of depression will increase to 5.75% of total burden of disease and it would be second cause of disability adjusted life years (DALYs) second only to ischaemic heart disease. **Objectives:** To assess the prevalence of depression in a rural population of productive age group using Patient Health Questionnaire-12 (PHQ-12) and to study various risk factors associated with depression. **Methods:** A community based cross sectional study was planned in field practice area of community medicine department S R T R Government Medical College, Ambajogai, Maharashtra. Systematic random sampling technique was used and a total 216 individuals between 20 to 60 years of age group were interviewed using a pretested structured Patient Health Questionnaire-12 after obtaining informed written consent. **Results:** Prevalence of depression was 36.57% in study subjects (52.43% Women and 26.86% men). Mild depression was present in 30.09% of study population followed by moderate depression (6.48%). Factors like Female gender, nuclear family, unmarried and others (which includes widowed, divorced, separated), lower socioeconomic status, those having associated co morbid conditions were found to be independent predictors of depression. **Conclusion:** Depression was found to be more prevalent in females than males in a rural population of productive age group. Depression, more specifically mild depression is a significant problem in rural population which needs to be addressed for effective implementation of mental health promotion.

**Key Word:** Depression, Patient Health Questionnaire-12 (PHQ-12).

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## INTRODUCTION

Health is pivotal for the growth, development, and productivity of a society and is vital for a happy and

healthy life. The definition of Health as per the World Health Organization includes physical, social, spiritual and mental health, and not merely an absence of disease or infirmity.<sup>1</sup> It has been stated that No Health without mental health.<sup>2</sup> This underlines the fact that mental health is an integral and essential component of health. Depression is a common mental disorder, characterized by persistent sadness and a loss of interest in activities that you normally enjoy, accompanied by an inability to carry out daily activities, for at least two weeks.<sup>3</sup> Depression is a disorder of major public health importance, in terms of its prevalence, suffering, dysfunction, morbidity and economic burden. It has been estimated that the burden of depression will increase to 5.75% of the total burden of disease and it would be

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second cause of disability-adjusted life years (DALYs) second only to Ischaemic heart disease.<sup>4</sup> Depression was found to be the most common disability in a study conducted by the World Health Organization in fourteen primary care settings worldwide.<sup>5</sup> Depression is estimated to affect 340 million people globally.<sup>6</sup> The prevalence of the psychiatric disorder is reported to differ between countries and within countries across various ethnicities.<sup>7</sup> In 2013, India accounted for 15% of global DALYs attributable to mental, neurological and substance use disorder (31 million DALYs) with depression accounting for 37% (11.5 million DALYs).<sup>8</sup> As per National Mental Health Survey 2015-16, the lifetime prevalence of depression in India was 5.25% among individuals aged 18+ years. WHO has declared World Health Day theme for the year 2017 as 'Depression - Let's talk'. In India, very few community-based studies have been conducted on depression in rural population of productive age group. With reference to above background, this study was conducted to provide data on the prevalence of depression in a rural population of productive age group using the Patient Health Questionnaire (PHQ-12) and study its associated risk factors.

## MATERIALS AND METHODS

A Community based cross-sectional study was carried out in rural field practice area of Swami Ramanand Teerth Rural Government Medical College, Ambajogai, Maharashtra. Duration of study was 3 months from 1<sup>st</sup> November 2017 to 31<sup>st</sup> January 2018.

### Inclusion criteria

1. Those individuals aged 20 to 60 years included in this study.
2. Those individuals willing to participate in the study.

### Exclusion criteria

1. Those individuals who reside in study area less than 6 months were excluded.
2. Individuals, more than 60 years of age were excluded.

**Sample size:** The Sample size was calculated by using formula  $n = \frac{z^2 pq}{d^2}$ , where n= Minimum sample size

required for the study,  $z = 1.96$ ,  $d$ - absolute precision ( $d = 0.05$ ),  $p$ - prevalence,  $q = 1-p$  and by taking 15% prevalence of depression.<sup>9</sup> Calculated sample size was 196. Considering 10% non-response rate, the corrected sample size was 216.

**Sampling Technique:** A total of 216 individuals were selected from our field practice area (sampling frame of 2185 individuals) by using systematic random sampling method and sampling interval of 10. 1<sup>st</sup> individual is selected from 1<sup>st</sup> 10 individuals of sampling frame by lottery method and then subsequent individuals were selected at interval of 10 till to get the required sample size of 216. The purpose of the study was explained to participants and written informed consent was taken from them in the local language. Data regarding socio-demographic factors such as age, sex, religion, education, marital status, type of family, occupation, socioeconomic status, and morbid condition etc; was collected using pre-designed and pre-tested proforma.

**A Tool used for assessment of depression:** Depression was assessed by using Patient Health Questionnaire (PHQ-12) whose reliability and validity as a screening tool was tested in Indians.<sup>10</sup> Patient Health Questionnaire-12 consists of 12 questions with a maximum score of 12. Each question has yes or no responses with 1 score for each yes response. Those who scored 4 or more were considered as having depression. Ethical clearance was obtained from the Institutional ethics committee of our college.

**Statistical Analysis:** Data was compiled and analyzed using Microsoft Excel, Epi Info version-6 software and SPSS-21. Frequency distributions were calculated for almost all independent variables. Odds ratio and its 95% confidence intervals were calculated. Chi-square test was used to determine statistical significance between Depression and independent variables and  $p < 0.05$  was considered to be as statistically significant. Those study participants who found moderate to severe depression were referred to college hospital for psychiatric evaluation and management.

## RESULTS

TABLE 1: Distribution of study participants according to Socio-demographic characteristics

| Variables |         | Frequency (n=216) | Percentage (%) |
|-----------|---------|-------------------|----------------|
| Age Group | (20-29) | 68                | 31.48          |
|           | (30-39) | 67                | 31.0           |
|           | (40-49) | 40                | 18.51          |
|           | (50-60) | 41                | 18.98          |
| Gender    | Male    | 134               | 62.03          |
|           | Female  | 82                | 37.96          |
| Religion  | Hindu   | 146               | 67.59          |

|                        |                        |     |       |
|------------------------|------------------------|-----|-------|
| Type of family         | Muslim                 | 43  | 19.90 |
|                        | Other                  | 27  | 12.50 |
|                        | Nuclear                | 48  | 22.22 |
|                        | Joint                  | 168 | 77.78 |
| Socioeconomic status # | Upper middle and above | 126 | 58.33 |
|                        | Middle class and below | 90  | 41.67 |
| Occupation             | Not working            | 14  | 6.48  |
|                        | Working                | 202 | 93.51 |
| Education status       | Illiterate             | 30  | 13.88 |
|                        | Literate               | 186 | 86.11 |
| Marital status         | Married                | 173 | 80.09 |
|                        | Unmarried and others*  | 43  | 19.90 |

# Modified BG Prasad Classification \* Others includes widow/widower/separated/divorced.

Table no 1 showed sociodemographic characteristics of study participants. Out of 216 study participants enrolled in the study, there were 134 males (62.03%) and 82 females (37.96%). The mean age of the study population was 36.6( $\pm 11.01$ ) years. Majority of the study population were Hindu (67.59%), working (93.5%), literate (86.1%), married (80.1%), living in a joint type of family (77.8%) and belonged to upper socioeconomic class (58.4%) as per modified B. G Prasad classification.

Table 2: Distribution of Study population on basis of PHQ-12 Score (N=216)

| Depression on basis of PHQ-12 Score | PHQ-12 Score | Number | Percentage |
|-------------------------------------|--------------|--------|------------|
| No Depression                       | (0-3)        | 137    | 63.42%     |
| Mild Depression                     | (4-6)        | 65     | 30.09%     |
| Moderate Depression                 | (7-9)        | 14     | 6.48%      |
| Severe Depression                   | (10-12)      | 00     | 00.00%     |

Table 2 shows the distribution of study population as per PHQ-12 SCORE. Out of 216 study respondents interviewed, 79 were having depression as per PHQ12 Score (36 male and 43 female), 30.09% of study population were having mild depression and 06.48% population having moderate depression. No study respondent showed severe depression.

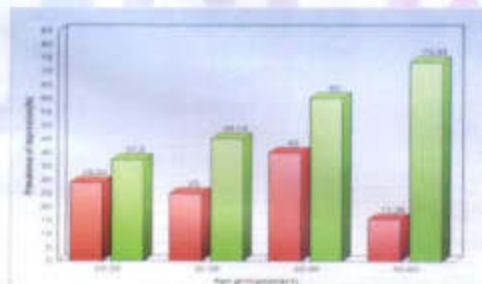


Figure 1: Age-wise and Gender wise distribution of depression in a rural population

Above bar diagram showed that the prevalence of depression among female was increased with increase in age but no such trend was observed in the male.

Table 3: Risk factors for depression (N=216)

| Sr. No | Variables      | Depression (%) | Total (%) | P value | OR(95% CI)         |
|--------|----------------|----------------|-----------|---------|--------------------|
| 1      | Age Group      |                |           |         |                    |
|        | (20-29)        | 21(30.9)       | 68(31.5)  | 0.249   | Reference          |
|        | (30-39)        | 23(34.3)       | 67(31.0)  |         | 0.774(0.342-1.754) |
|        | (40-49)        | 20(50.0)       | 40(18.5)  |         | 0.906(0.403-2.039) |
|        | (50-60)        | 15(36.6)       | 41(18.9)  |         | 1.733(0.713-4.211) |
| 2      | Gender         |                |           |         |                    |
|        | Male           | 36(26.9)       | 134(62)   | 0.0001* | 3.001(1.684-5.348) |
|        | Female         | 43(52.4)       | 82(37.9)  |         |                    |
| 3      | Religion       |                |           |         |                    |
|        | Hindu          | 52(35.6)       | 146(67.6) | 0.895   | Reference          |
|        | Muslim         | 17(39.5)       | 43(19.9)  |         | 0.940(0.401-2.203) |
|        | Other          | 10(37.0)       | 27(12.5)  |         | 1.112(0.412-2.997) |
| 4      | Type of family |                |           |         |                    |
|        | Joint          | 53(31.5)       | 168(77.8) |         |                    |



|   |                        |          |           |         |                    |
|---|------------------------|----------|-----------|---------|--------------------|
| 5 | Nuclear                | 26(54.1) | 48(22.3)  | 0.004*  | 2.564(1.333-4.934) |
|   | Upper middle and above | 37(29.4) | 126(58.4) |         |                    |
| 6 | Middle class and below | 42(46.7) | 90(41.7)  | 0.009*  | 2.105(1.197-3.701) |
|   | Working                | 74(36.6) | 202(93.5) |         |                    |
| 7 | Not working            | 05(35.7) | 14(6.5)   | 0.944   | 0.961(0.310-2.975) |
|   | Literate               | 62(33.3) | 186(86.1) |         |                    |
| 8 | Illiterate             | 17(56.7) | 30(13.9)  | 0.013*  | 2.615(1.194-5.727) |
|   | Married                | 54(30.9) | 173(80.1) |         |                    |
| 9 | Unmarried and others   | 25(58.1) | 43(19.9)  | 0.001*  | 3.061(1.542-6.071) |
|   | Absent                 | 54(30.9) | 175(81.0) |         |                    |
|   | Present                | 25(60.9) | 41(18.9)  | 0.0003* | 3.501(1.731-7.084) |

\*p value significant

Table 3 shows that the females were more likely to suffer from depression as compared to male ( $p=0.000$ ). The study subjects living in a nuclear type of family were 2.56 times more likely to suffer from depression as compared to those living in a joint type of family( $p=0.004$ ). The other variables that had a significant association with prevalence of depression were the lower socioeconomic class (middle class and below), illiterates, those living alone without a spouse i.e., unmarried, widowed, divorced, and presence of other co-morbid conditions. There was no significant association between age ( $p=0.249$ ), religion ( $p=0.895$ ), and occupation ( $p=0.944$ ) and the prevalence of depression.

Table4: Multivariate analysis of the association of risk factors with depression

|                      | Variables              | Depression No (%) | OR(95%CI)           | P value |
|----------------------|------------------------|-------------------|---------------------|---------|
| Age Group            | (20-29)                | 21(30.88)         | Reference           |         |
|                      | (30-39)                | 23(34.32)         | 0.923(0.319-2.672)  | 0.883   |
|                      | (40-49)                | 20(50)            | 0.911(0.339-2.445)  | 0.852   |
|                      | (50-60)                | 15(36.58)         | 0.546(0.187-1.595)  | 0.269   |
| Gender               | Male                   | 36(26.86)         | Reference           |         |
|                      | Female                 | 43(52.43)         | 2.701(1.358-5.372)  | 0.005*  |
|                      | Hindu                  | 52(35.61)         | Reference           |         |
| Religion             | Muslim                 | 17(39.53)         | 0.924(0.338-2.528)  | 0.878   |
|                      | Other                  | 10(37.03)         | 1.024(0.312-3.359)  | 0.969   |
| Type of family       | Joint                  | 53(31.54)         | Reference           |         |
|                      | Nuclear                | 26(54.16)         | 0.341(0.153-0.758)  | 0.008*  |
| Socioeconomic status | Upper middle and above | 37(29.36)         | Reference           |         |
|                      | Middle class and below | 42(46.66)         | 2.758(1.368-5.561)  | 0.005*  |
| Occupation           | Working                | 74(36.63)         | Reference           |         |
|                      | Not working            | 05(35.71)         | 0.999(0.225-4.427)  | 0.999   |
| Education status     | Literate               | 62(33.33)         | Reference           |         |
|                      | Illiterate             | 17(56.67)         | 0.441(0.173-1.120)  | 0.085   |
| Marital status       | Married                | 54(30.85)         | Reference           |         |
|                      | Unmarried and Others   | 25(58.13)         | 5.107(2.145-12.158) | 0.000*  |
| Co-morbid Condition  | Absent                 | 54(30.85)         | Reference           |         |
|                      | Present                | 25(60.98)         | 4.792(2.034-11.293) | 0.000*  |

\*p value significant

Table 4 shows the result of multiple logistic regression analysis. Multiple logistic regression analysis revealed that in our study population, Female gender, nuclear family, unmarried and others (which includes widowed, divorced, separated), lower socioeconomic status, those having associated co morbid conditions were found to be independent predictors of depression. Age, religion, education status, occupational status was not found to have a significant effect on the prevalence of depression.



## DISCUSSION

As per PHQ-12 SCORE of 4 or more, the prevalence of depression in a rural population of productive age group was found to be 36.57%. The similar result was revealed by study conducted in a rural area of Ahmednagar district, Maharashtra.<sup>11</sup>

Table 5: Different studies on depression

| Sr.No | Study                            | Place                           | Sample Size | Screening tool used for depression   | Prevalence of depression |
|-------|----------------------------------|---------------------------------|-------------|--------------------------------------|--------------------------|
| 1     | Soni S <i>et al</i> , 2016       | Bihar, India                    | 450         | Geriatric Depression scale           | 39.6%                    |
| 2     | Sengupta P <i>et al</i> , 2015   | Ludhiana, India                 | 3038        | Geriatric Depression scale           | 8.9%                     |
| 3     | Poongothai S <i>et al</i> , 2009 | Chennai, India                  | 25455       | Patient Health Questionnaire(PHQ-12) | 15.1%                    |
| 4     | Goyal A <i>et al</i> 2014        | Faridkot, Panjab                | 100         | Geriatric Depression scale           | 77%                      |
| 5     | Prachet R <i>et al</i> , 2013    | Dharwad, Karnataka, India       | 218         | Geriatric Depression scale           | 29.4%                    |
| 6     | Rajkumar AP <i>et al</i> , 2009  | Vellore, India                  | 1000        | Geriatric Mental State               | 12.7%                    |
| 7     | Kamble SV <i>et al</i> , 2009    | Ahmednagar, Maharashtra, India  | 494         | Goldberg and Bridges' scale          | 31.4%                    |
| 8     | Sinha SP <i>et al</i> , 2013     | Kancheepuram, Tamil Nadu, India | 103         | Geriatric Depression scale           | 42.7%                    |
| 9     | Jain RK <i>et al</i> , 2007      | Mumbai, India                   | 196         | Geriatric Depression scale           | 45.9%                    |
| 10    | Taqi AM <i>et al</i> 2007        | Karachi, Pakistan               | 400         | Geriatric Depression scale           | 19.5%                    |
| 11    | Present study                    | Ambajogal, Maharashtra, India   | 216         | Patient Health Questionnaire(PHQ-12) | 36.6%                    |

Table 5 shows different studies on depression from various regions. The much lower result was revealed in studies conducted by Sengupta *et al* (8.9%), Prachet *et al* (29.36%), Rajkumar *et al* (12.7%), Taqui *et al* (19.5%).<sup>12-14,18</sup> Compared to the present study, the result of other studies was much higher.<sup>15-17</sup> Baseline characteristics of the study population, the different tool used for assessment of depression and different sample size might be contributed to this wide variation in the prevalence of depression. Female gender, nuclear family, low socioeconomic status, Illiterate, those living alone without spouse (unmarried/widow/separated/divorced) are associated with depression. Similar findings were observed by Sengupta *et al* and Kamble *et al*.<sup>11-12</sup> On multiple logistic regression analysis, the present study revealed that Female gender, nuclear family, those living alone without spouse, low socio economic status, associated comorbid conditions were strong predictor of depression where as Sengupta *et al* observed only female gender and nuclear family as predictor of depression.<sup>12</sup> The present study revealed that co morbid condition is associated with depression. A similar finding was seen in Prachet *et al*.<sup>13</sup> There was no significant association between depression and Gender, co morbid conditions in Goyal *et al*.<sup>17</sup>

## CONCLUSION

The prevalence of depression in a rural population of productive age group was 36.57%. We found that

socioeconomic factors and morbid conditions were major risk factors for depression. Depression, more specifically mild depression is a significant problem in rural population which needs to be addressed for effective implementation of mental health promotion. Such kind of study helps to persuade family physician regarding the importance of early detection and treatment of depression. Early detection is probably the first step in the pathway to manage depression and this need to happen in variety of settings like homes, workplaces, educational institutions, health care and community settings through informed and trained persons.

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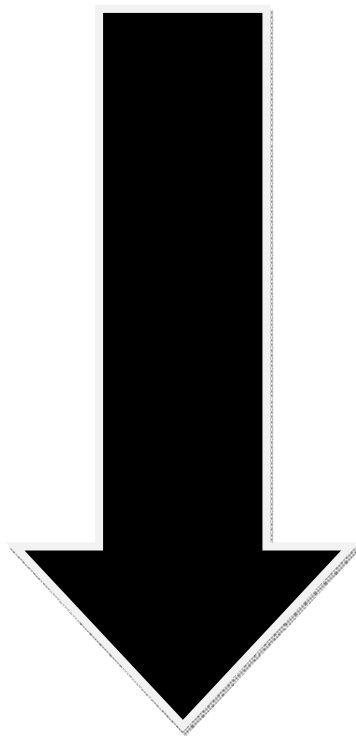
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Table 3 show subjects living in a depression w i.e., unmarried between age t

Table 4 show study population lower socioeconomic depression. / prevalence of

# Orthopedics Publications 2019





# Knowledge, attitude and practices of generic names usage in prescription among the medical postgraduate residents of a tertiary care teaching hospital: an observational cross-sectional study

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## ABSTRACT

**Background:** Establishment of Pradhan Mantri Bhartiya Janaushadhi Kendras through Pradhan Mantri Janaushadhi Pariyojana (PMBJP) is a breakthrough step to reduce expenses in healthcare due to costly branded names in prescription. Medical council of India also amended clause 1.5 of the Indian Medical Council Regulations, 2002 mandating the doctors to prescribe medicines by generic names in place of brand names. Moreover, medical practitioner nowadays has raised concern about education/qualification of the chemist who is being made the decision maker.

**Methods:** In this questionnaire based cross-sectional observational study, all students admitted to post graduation course in academic year 2018 were included and those who were not willing to give consent were excluded from study. A knowledge, attitude and practices (KAP) questionnaire containing 12 questions was assessed by using true/false type and Likert scale-based questions. Descriptive statistics used to generate frequencies, percentages and proportions.

**Results:** Majority of the population have answered positively about knowledge questions. Surprisingly 72.41% population don't know about process of new drug approval. Most of them agreed to pros and cons of generic drug prescribing. 58.14% population always write generic names in their prescription. Shockingly 74.42% population write prescription based on their knowledge from promotional literature by a medical representative.

**Conclusions:** Findings of present study highlights usefulness of the practice of writing generic names in prescriptions. It also raises concern about professional qualification of the chemist who will be decision maker in drug delivery to consumers.

**Keywords:** Attitude, Generic, Janaushadhi, Knowledge, Practice, Prescription

## INTRODUCTION

Generic or non-proprietary name is the name for the active ingredient in the medicine that is decided by an expert committee and is understood internationally. These drugs are usually interchangeable with branded drugs and do not require licence for their manufacturing. Basically, these drugs are marketed after the expiry date of the patent or other exclusive rights.<sup>1</sup> Writing costly branded names in prescription seldom leads to expensive and unaffordable

treatment.<sup>2,3</sup> Establishment of Pradhan Mantri Bhartiya Janaushadhi Kendras through Pradhan Mantri Bhartiya Janaushadhi Pariyojana (PMBJP) is a breakthrough step to reduce out of pocket expenses in healthcare.<sup>4</sup> Medical council of India also amended clause 1.5 of the Indian Medical Council (Professional Conduct, Etiquette and Ethics) Regulations, 2002 mandating the doctors to prescribe medicines by generic names in place of brand names.<sup>5</sup> Prescribing generics whenever the outcome sought is clinical or easily measurable like drugs for pain,



blood pressure, infections, and so forth will surely reduce treatment cost. While switching to generics may lead to therapeutic failure in drugs requiring careful titration and close tolerances like anticonvulsants, antifungals, thyroid replacement, and others.<sup>6</sup> Moreover, medical practitioner nowadays have raised concern about education/qualification of the chemist who is being made the decision maker. This chemist empowerment could increase prices as they may sell brands with higher absolute margins.<sup>7</sup>

With this background, this questionnaire based cross sectional study is designed to assess knowledge, attitude and practice about generic drug names usage in prescription.

## METHODS

This questionnaire based cross sectional observational study was conducted at Department of Pharmacology, Swami Ramanand Teerth Government Rural Medical College, Ambajogai, Maharashtra, India with study objective to assess the existing knowledge, attitude and practices of post graduate students on generic drug names usage in prescription. All the students admitted to post graduation course in academic year 2018 were included in this study. Those who were not willing to give consent were excluded from study. After explaining the benefits and risks of participation in the study to each subject to the fullest extent possible about the study, in language and terms they are able to understand; the investigator obtained written informed consent from all the participants prior to entering the study. All the participant was gathered on the day of data collection. A KAP questionnaire containing 12 questions (knowledge 04, attitude 04, and practice 04) was given to each participant. They were provided 5 minutes to fill the questionnaire. Participants taking extra time were excluded from the study. The participants KAP was assessed by using true/false type and a Likert scale-based question whose responses ranged from “strongly agree” to “strongly disagree” and “always” to “never.”

Statistical analysis was done using Graph Pad Prism Software Version 6. Simple descriptive statistics were used to generate frequencies, percentages and proportions.

## RESULTS

Total 43 doctors participated in this study. Among them 19 were males and 24 females. The analysis was done using five-point response options of the Likert scale for attitude and practice questionnaire and true or false type options for assessing knowledge.

All participants know that generic drugs are cheaper than branded drugs. Majority, about 72.41% participants know that generic and branded drugs are equipotent. Surprisingly only 27.59% participants know about new drug development process and majority 72.41% failed to answer question about new drug approval correctly. Nearly 86.21% participants aware about new pharmaceutical policy 2017 (Table 1).

**Table 1: Knowledge questionnaire.**

| Knowledge Questionnaire  | True (%) | False (%) |
|--|----------|-----------|
| Generic drugs are cheaper than branded drugs.                                      | 100      | 0         |
| Generic drugs are low in potency and efficacy compared to branded drugs.           | 27.59    | 72.41     |
| Newly approved drugs are available as branded drugs only.                          | 27.59    | 72.41     |
| New pharmaceutical policy 2017 recommends use of e-prescription for generic drugs. | 86.21    | 13.79     |

Majority (95.02%) of participants believe that writing generic names in prescription is a good practice and must be made mandatory. Most of them (86.05%) also believe that this practice will help in establishing a transparent doctor patient relationship.

On the other hand, majority (65.12%) were concerned about usefulness and availability of generic drugs in all clinical conditions, while 76.75% think that writing generic names in prescription will give liberty to pharmacist to select any available brand which will be more profitable for him. About 6.98% to 13.95% participants were undecided about their attitude (Table 2).

**Table 2: Attitude questionnaire.**

| Practice of writing generic names in prescription   | Strongly agree (%) | Agree (%) | Undecided (%) | Disagree (%) | Strongly disagree (%) |
|---|--------------------|-----------|---------------|--------------|-----------------------|
| Is a good practice and must be made mandatory?  | 25.58              | 67.44     | 6.98          | 0            | 0                     |
| Is impossible in some medical conditions.   | 2.33               | 62.79     | 13.95         | 16.28        | 4.65                  |
| Along with generic drug stores will help in establishing a transparent doctor patient relationship. | 16.28              | 69.77     | 11.63         | 2.33         | 0                     |
| Will provide liberty to pharmacist to supply from various available brands.                         | 16.28              | 60.47     | 13.95         | 9.3          | 0                     |

In practice questionnaire, majority of the participants shown positive response about consideration of cost before prescribing and allowing patients to choose among various available brands.

Surprisingly large proportion of participants (90.70%) rely on promotional literature for knowledge upgradation and don't consider other sources of drug information (Table 3).

**Table 3: Practice questionnaire.**

| Practice questionnaire   | Always (%) | Usually (%) | Sometimes (%) | Seldom (%) | Never (%) |
|--|------------|-------------|---------------|------------|-----------|
| Do you consider cost of a drug before prescribing?                                     | 74.42      | 11.63       | 11.63         | 0          | 2.33      |
| Do you update your knowledge with promotional literature by a medical representative?  | 46.51      | 27.91       | 16.28         | 4.65       | 4.65      |
| Do you allow patients to choose among different available brands of a particular drug? | 46.51      | 18.6        | 16.28         | 6.98       | 11.63     |
| Do you write generic names in your prescription?                                       | 58.14      | 27.91       | 6.98          | 4.65       | 2.33      |

## DISCUSSION

In the present study, good percentage of participants have considerable knowledge about generic medicines, and they have positive attitude about the safety, efficacy and quality of generic medicines.

Fortunately, the Indian context is better than that noted in other countries. In a study conducted in Auckland, New Zealand, only 51% of the respondents had heard of the phrase "generic drug."<sup>8</sup> Naing C et al, assessed knowledge of the medications taken by the population of Malaysia, noting that 85.8% did not know the term "generic drug", 86.3% did not know how to reply on the quality of generic drugs compared to reference drugs and 86.9% did not know about price differences between generic and reference drugs.<sup>9</sup> The good results obtained among the Indian population can be attributed to awareness-heightening and popularization programs for generic drugs, run by the Indian Government and the pharmaceutical companies producing these types of medications. All participants are aware of Jan Aushadhi scheme of Govt. of India whose purpose is to set up generic drug stores around the country which is contrary to the finding of Badwaik R et al, (Table 1).<sup>10</sup>

High numbers of participants agree that to reduce overall health expenditure generic medicines are an important tool. The cost of generic medicines has been found to be up to 91% less than that of the innovator medicine in India.<sup>11-13</sup>

In this study, most of the respondents believed in efficacy of generics and being bioequivalent to their innovator counterparts they can be interchangeable with a branded drug. Similar findings were obtained by Thomas R et al, Davit BM et al. and Gupta S et al.<sup>14-16</sup>

Many participants believe that prescribing generic drugs is impossible in some clinical conditions due to non-availability or less efficacy (Table 2). However, this effect is not exclusive to generics. This may also be blamed on inter-individual variations, which is a serious problem consisting of a loss of pharmacological efficacy and adverse effects. Some of the factors associated with the variability of the pharmacological and therapeutic effects, are age, pregnancy and the presence of disease.<sup>17</sup> In fact, there are situations in which a specific medication may present a therapeutic response other than the expected outcome or the patient may even be refractory to pharmacological treatment in some cases. For example, one third of patients with depression are refractory to pharmacological treatment.<sup>18</sup>

In present study, author have found that most of the doctors prescribe generic medicines. These findings are similar to that of Gupta S et al.<sup>16</sup> Many admitted that most of the times their prescriptions are influenced by promotional literature and they believe that they prescribe branded drugs which is similar to the finding of another study (Table 3).<sup>10</sup>

Surprisingly only 27.59% participants know about new drug development process and majority 72.41% failed to answer question about new drug approval correctly. This finding suggested strong need of knowledge upgradation of health care providers (Table 1).

Small sample size is the major limitations of this study. Thus, findings of this study cannot be generalized. Author have only studied the doctor's perception and understanding regarding generic medicines. It would be appropriate to analyse the perception and understanding of other health care professionals as well as patients.

## CONCLUSION

In spite of shortcomings the findings of present study cannot be neglected. The data about knowledge, attitude and practice of post graduate resident doctors about writing generic names in prescriptions is generated through this study. Without doubt it highlights usefulness of this practice. It also raises concern about professional qualification of the chemist who will be decision maker in drug delivery to consumers. Study also recommends need of knowledge upgradation of health care providers.

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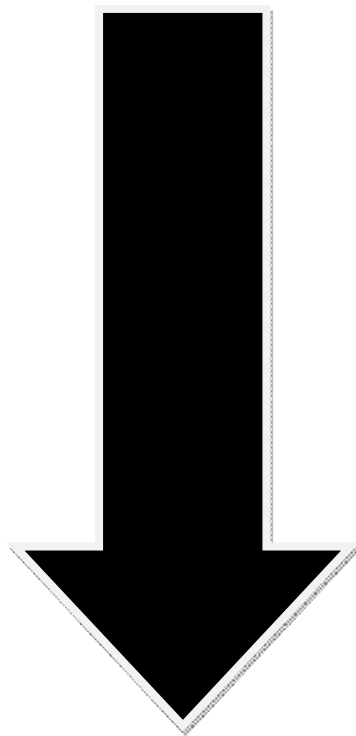
*Ethical approval: The study was approved by the Institutional Ethics Committee Swami Ramanand Teerth Government Rural Medical College, Ambajogai, Maharashtra, India*

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# Pharmacology Publications 2019





# Study of drug prescription pattern and adverse drug reaction monitoring in patients with hypertension and diabetes visiting outpatient department in a government tertiary care hospital in Maharashtra, India

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## ABSTRACT

**Background:** Drug utilization study is an important tool to study the clinical use of drugs and its impact on healthcare system. DUS in patients with HTN and DM is essential to observe the changing prescribing attitude of physicians with the aim to promote rational use of drugs and to minimize the adverse drug reactions. **Methods:** A cross sectional observational study was conducted on randomly selected patients attending medicine outpatient department in a tertiary care hospital. Drug prescription sheets of 600 patients were studied for 18 months from January 2016 to June 2017 and the prescribing pattern was analysed using the World Health Organization basic drug indicators.

**Results:** Total 2029 drugs were prescribed to 600 patients that belonged to various classes. The average number of drugs prescribed per encounter was 3.4. Majority (61.5%) drugs were prescribed using generic names. Percentage encounters with the antibiotics and injections were 6.3 and 11.5 per cent respectively. 38% drugs were prescribed from the 20th edition of WHO Model List of Essential Medicines. PDD in the current study was found to be significantly less than WHO DDD in all drugs. All of the prescriptions in the present study conformed to WHO guidelines and majority of them with JNC VIII guidelines.

**Conclusions:** The findings of this study are comparable to those of other studies. However, there is a scope of improvement in areas such as overdosing, prescribing more by generic names instead of brand names and from WHO Model List of Essential Medicines.

**Keywords:** Defined daily dose, Drug utilization, Essential medicines, Generic drugs, Overdosing, Prescribed daily dose

## INTRODUCTION

Hypertension (HTN) and Diabetes mellitus (DM) are both independent risk factors for ischemic heart disease but hypertension associated with Non-Insulin Dependent Diabetes Mellitus (insulin resistance and hyperinsulinemia) is likely to accelerate the process of atherogenesis.<sup>1</sup> In recent years, adequate data from well-

designed randomized clinical trials have demonstrated the effectiveness of aggressive treatment of hypertension in reducing both complications associated with diabetes and the need for retinal photocoagulation.<sup>2</sup>

Therapeutic guidelines have been issued by the WHO and Joint National Committee (JNC VIII) which emphasizes control of systolic blood pressure (SBP) and diastolic

blood pressure (DBP) with age and comorbidity specific treatment cut-offs. The adherence of physicians to such guidelines can be evaluated by drug utilization studies.

HTN and Diabetes Mellitus frequently coexist specially with increasing age. HTN is about twice as common in patients with DM than in those without (8%). In Helsinki's heart prevalence study, incidence of HTN is 30% amongst NIDDM patients.<sup>3</sup> Thus drug utilization studies carried out at frequent intervals to evaluate and analyse the drug therapy in Hypertension associated with Non-Insulin Dependent Diabetes Mellitus (NIDDM) is very essential to observe the changing prescribing attitude of physicians with the aim to promote rational use of drugs and to minimize the adverse drug reactions (ADRs).<sup>4</sup> This study is proposed to evaluate the utilization pattern of drugs prescribed for HTN with DM in adult patients attending out-patient department (OPD) in a government tertiary care hospital in Maharashtra, the compliance of drug prescriptions with Standard Treatment Guidelines and side effects, if any, will be recorded.

## METHODS

This was a cross sectional observational study conducted on randomly selected patients attending outpatient department (OPD) of medicine in a tertiary care teaching hospital. Institutional Ethics Committee approval was obtained prior to the conduction of the study. Total of 600 patients were enrolled in the study as per the following inclusion and exclusion criteria over a period of 18 months from January 2016 to June 2017. Data was obtained from the drug prescription sheets of hypertensive diabetic patients of age 35 years or more attending medicine OPD.

### Inclusion criteria

- Patients having diabetes and hypertension.
- Patients with age 35 years or more.
- Patients with co-morbidities related to HTN and DM.
- Patients visiting the outpatient department

### Exclusion criteria

- Patient not willing to consent for the study.
- Patients receiving drugs for diseases other than HTN, DM and their complications.
- Patients having end organ damage at the time of diagnosis of HTN and DM.

The treatment given was segregated for various WHO DUS indicators such as average number of drugs per encounter, percentage of drugs prescribed by generic/brand name, percentage of various routes of drug administration, percentage of drugs prescribed in fixed dose combinations and percentage of drugs prescribed from WHO model list of essential medicines. The drugs were classified according to the anatomical therapeutic classification based on their chemical, pharmacological, and therapeutic properties. The drug utilization was

measured using parameters such as Defined daily dose (DDD), prescribed daily dose (PDD), and PDD/DDD ratio.

## Calculations

Drug usage in our study was obtained using following formula

### Drug usage (DDD):

$$= \frac{\text{Items issued} \times \text{Amount of drug per item}}{\text{WHO DDD}}$$

Prescribed Daily Dose (PDD) in our study is calculated using formula:

### Prescribed Daily Dose (PDD):

$$= \frac{\text{Total number of dosage units prescribed} \times \text{Strength of each unit} \times 1000}{\text{DDD} \times \text{Study duration} \times \text{Sample size}}$$

## Statistical analysis

Statistical analysis was done by using Microsoft office Excel 2007.

## RESULTS

It was observed that out of total 600 patients, 322(54%) were males and 278 (46%) were females. The mean age of the study population was 62 years. Majority of the patients belonged to the age group of 61 years to 70 years which constituted 40% of the total study population. Total 2029 drugs were prescribed to 600 patients that belonged to various classes of anti-diabetic and anti-hypertensive drugs. Some prescriptions also consisted of drugs for the treatment of other co-morbidities and complaints. The minimum and maximum numbers of drugs per prescription were 2 and 9 respectively. Out of the total drugs prescribed, 92 (4.5%) were fixed drug combinations (FDCs) and out of total prescriptions of 600, 15.3% consisted of FDCs as summarised in Table 1.

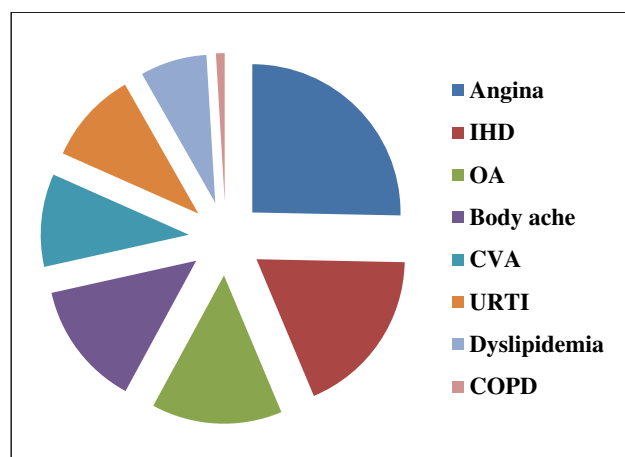
**Table 1: Distribution of FDCs among various classes of drugs.**

| Class                   | FDCs | Percentage |
|-------------------------|------|------------|
| Anti-diabetic Drugs     | 17   | 18.5       |
| Anti-hypertensive Drugs | 20   | 21.7       |
| Others                  | 56   | 60.9       |
| Total FDCs              | 92   | 100        |

Combination of Atorvastatin and Aspirin was the most common FDC. In treatment of co-existing diabetes and hypertension, multiple drugs were prescribed, the minimum number was two and maximum was five.

Out of all the combinations prescribed for the treatment of DM and HTN, biguanides along with calcium channel blockers was most commonly prescribed combination followed by Biguanides and Angiotensin Converting Enzyme Inhibitors. Metformin was most commonly prescribed Biguanides and Amlodipine was most commonly prescribed Calcium Channel Blocker.

Drugs were also prescribed for some other diseases along with DM and HTN. The percentage of presence of these illnesses in total sample population of our study is summarised in the Figure 1.



**Figure 1: Diseases treated other than DM and HTN.**

As shown in the Figure 1, the most common diseases presenting along with diabetes and hypertension, in this study are Unstable Angina and Ischemic heart disease. The commonly reported complaints were gastric discomfort (2.3%) and cough (2.2%). Some not so common were palpitations, loose motions and constipation.

#### WHO core drugs use indicators

The average number of drugs prescribed per encounter in our study was 3.4 considering the total number of drugs prescribed to be 2029.

#### Percentage of drugs prescribed by generic name/brand name

Around 60% of drugs were prescribed by their generic names (Table 2).

As shown in Table 2, 47 (61.5%) drugs were prescribed using generic names and 782 (38.5%) drugs were prescribed using brand names.

Out of all the anti-diabetic drugs prescribed, majority were prescribed by their brand names (56.5%) and majority of antihypertensive drugs were prescribed using generic names (90%). Various other WHO core drug indicators studied are mentioned in the Table 3.

#### Percentage of drugs prescribed from the essential drug list and from the hospital dispensary list

Out of 63 different drugs, 24 (38%) were from the 20th edition of WHO Model List of Essential Medicines and 33 (52%) were from the National List of Essential Medicines of India, 2016. 25 drugs (40%) were from hospital formulary list.

**Table 2: Number of drugs prescribed by generic name/ brand name.**

| Route                   | Drugs prescribed by generic name | Drugs prescribed by brand name | Total |
|-------------------------|----------------------------------|--------------------------------|-------|
| Anti-diabetic drugs     | 361                              | 468                            | 829   |
| Anti-hypertensive drugs | 611                              | 65                             | 676   |
| Others                  | 275                              | 249                            | 524   |
| Total                   | 1247                             | 782                            | 2029  |

**Table 3: WHO core drug indicators.**

| Total encounters | Core drug indicator                        | Encounters | Percentage |
|------------------|--|------------|------------|
| 600              | Percentage encounters with the antibiotic  | 38         | 6.3        |
| 600              | Percentage of encounters with an injection | 69         | 11.5       |

#### Drug use pattern as per ATC/DDD system

The ATC codes and DDD of the drugs commonly prescribed was found using the WHO reference DDDs and ATC codes website and is mentioned in Table 4.

The DDD and PDD for drugs commonly prescribed in this study were calculated and are mentioned in Table 5. It is also important to take into consideration the difference between PDD and DDD, if found to be substantial, when evaluating and comparing drug utilization figures.

Appropriateness of the prescriptions was analysed using Joint National Committee (JNC VIII) and World Health Organization guidelines for the management of diabetic hypertensive patients. Various combinations of antihypertensives and antidiabetics were used in the sample population. All of the prescriptions in the present study conformed to WHO guidelines. Majority of prescription were also conforming with JNC VIII guidelines except a few as shown in Figure 2.

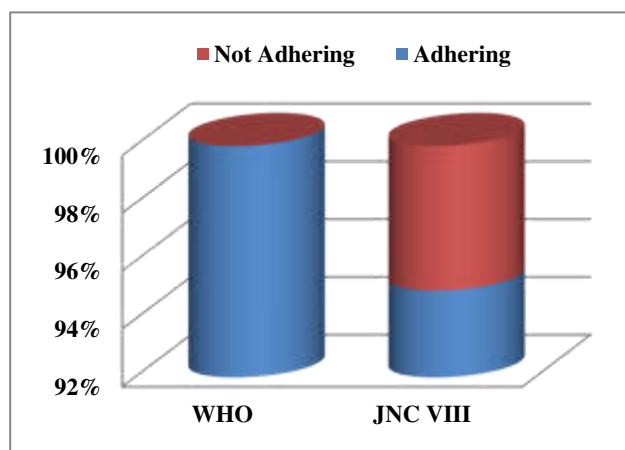


**Table 4: ATC codes and DDD of the drugs commonly prescribed.**

| Sr. No. | Name of drug         | Route of drug administration | ATC code | WHO DDD (gm) |
|---------|----------------------|------------------------------|----------|--------------|
| 1.      | Insulin              | Injection                    | A10AE01  | 40 U         |
| 2.      | Glimepiride          | Oral                         | A10BB12  | 2 mg         |
| 3.      | Metformin            | Oral                         | A10BA02  | 2g           |
| 4.      | Glibenclamide        | Oral                         | A10BB01  | 10 mg        |
| 6.      | Voglibose            | Oral                         | A10BF01  | Not defined  |
| 7.      | Pioglitazone         | Oral                         | A10BG03  | 30 mg        |
| 8.      | Enalapril            | Oral                         | C09AA02  | 10 mg        |
| 9.      | Telmisartan          | Oral                         | C09CA07  | 40mg         |
| 10.     | Amlodipine           | Oral                         | C08CA01  | 5 mg         |
| 11.     | Hydrochlorothiazide  | Oral                         | C03AA03  | 20 mg        |
| 12.     | Furosemide           | Oral                         | C03CA01  | 40 mg        |
| 13.     | Spironolactone       | Oral                         | C03DA01  | 75 mg        |
| 14.     | Torsemide            | Oral                         | C03CA04  | 15 mg        |
| 15.     | Metoprolol           | Oral                         | C07AB02  | 0.15 g       |
| 16.     | Atenolol             | Oral                         | C07AB03  | 75 mg        |
| 17.     | Carvedilol           | Oral                         | C07AG02  | 37.5 mg      |
| 18.     | Betaxolol            | Oral                         | C07AB05  | 20 mg        |
| 19.     | Amoxicillin          | Oral                         | J01CA04  | 1 g          |
| 20.     | Aspirin              | Oral                         | B01AC06  | 1 tablet     |
| 21.     | Atorvastatin         | Oral                         | C10AA05  | 20 mg        |
| 22.     | Diclofenac           | Oral                         | M01AB05  | 0.1 g        |
| 23.     | Ranitidine           | Oral                         | A02BA02  | 0.3 g        |
| 24.     | Isosorbide Dinitrate | Oral                         | C01DA08  | 60 mg        |

**Table 5: DDD and PDD of drugs prescribed in our study.**

| Name of drug         | ATC code | WHO DDD (gm) | Drug use in current study | Prescribed Daily Dose |
|----------------------|----------|--------------|---------------------------|-----------------------|
| Insulin              | A10AE01  | 40 U         | 477                       | 0.182648              |
| Glimepiride          | A10BB12  | 2 mg         | 4132.5                    | 0.009132              |
| Metformin            | A10BA02  | 2 g          | 405                       | 0.000046              |
| Glibenclamide        | A10BB01  | 10 mg        | 195                       | 0.000009              |
| Voglibose            | A10BF01  | Not defined  | -                         | -                     |
| Pioglitazone         | A10BG03  | 30 mg        | 75                        | 0.000137              |
| Enalapril            | C09AA02  | 10 mg        | 1897.5                    | 0.000046              |
| Telmisartan          | C09CA07  | 40mg         | 735                       | 0.000183              |
| Amlodipine           | C08CA01  | 5 mg         | 5760                      | 0.000023              |
| Hydrochlorothiazide  | C03AA03  | 20 mg        | 37.5                      | 0.000091              |
| Furosemide           | C03CA01  | 40 mg        | 172.5                     | 0.000183              |
| Spironolactone       | C03DA01  | 75 mg        | 40                        | 0.000342              |
| Torsemide            | C03CA04  | 15 mg        | 20                        | 0.000068              |
| Metoprolol           | C07AB02  | 0.15 g       | 12.5                      | 0.000685              |
| Atenolol             | C07AB03  | 75 mg        | 1140                      | 0.000342              |
| Carvedilol           | C07AG02  | 37.5 mg      | 8.75                      | 0.000171              |
| Betaxolol            | C07AB05  | 20 mg        | 15                        | 0.000091              |
| Amoxicillin          | J01CA04  | 1 g          | 125                       | 0.004566              |
| Aspirin              | B01AC06  | 1 tablet     | 1200                      | 0.004566              |
| Atorvastatin         | C10AA05  | 20 mg        | 2070                      | 0.000091              |
| Diclofenac           | M01AB05  | 0.1 g        | 832.5                     | 0.000457              |
| Ranitidine           | A02BA02  | 0.3 g        | 352.5                     | 0.001370              |
| Isosorbide Dinitrate | C01DA08  | 60 mg        | 102.5                     | 0.000274              |



**Figure 2: Adherence to JNC VIII guidelines.**

Angiotensin Converting enzymes and angiotensin receptor blockers, recommended as first line agents in diabetic hypertensive patients were prescribed in only 298 (49.7%) prescriptions. Also, it was observed that in none of the prescriptions, were the patients advised any form of life-style changes, dietary modifications or physical exercises along with the prescribed medications. In the current study, 600 prescription sheets of diabetic hypertensive patients attending medicine outpatient department and satisfying all the inclusion criteria were analysed.

## DISCUSSION

### *Demographic characteristics of study population*

In this study it was observed that majority of the patients suffering from diabetes and hypertension belonged to the age group of 61 to 70 years (39.5%) the mean age was 62 years. This corroborates with the results of the study conducted by Sweileh et al, in which the mean age of the patients was 64 years.<sup>5</sup> It may be because of the increasing inactivity, obesity and stress along with increasing age.

In this study it was observed that males (53.7%) were more commonly affected as compared to females (46.3%). Similar finding was observed in the studies conducted by Hussain et. al. and Shah et al, where the males were seen to be more commonly affected than females with the percentage of affected males being 56.4% and 52% respectively.<sup>6,7</sup> The reason for higher prevalence of diabetes and hypertension in males as compared to females may be because of the lifestyle differences among both such as higher consumption of alcohol by males along with occupational stress.

### *Drug prescribing pattern in study population*

In the current study total 2029 drugs were prescribed, it was found that average drug per prescription was 3.4 which was less as compared to the that in the study conducted by Sandozi et al (4.7%) and greater than that in the study conducted by Sweileh et al (1.42).<sup>4,7</sup> This

difference may be because of the varied demographic profiles of the sample population and variation in the prescribing habits of the practitioners.

In prescribing practices, average drug per prescription is an important tool. It is higher, 3.4 in this study as compared to the recommended limit of two drugs per encounter and the international average of 2.2 drugs per prescription.<sup>8</sup> The prescribing trend in the present study is suggestive of polypharmacy. Polypharmacy, is known to be associated with significant drug interactions, adverse drug reactions and consequently a potential for increased hospital admissions. The possible reason for this practice could be lack of accuracy in diagnosis, easy availability of multiple drugs or lack of awareness of various guidelines for treatment. However, this study consisted of analysis of two diseases coexisting, which necessitates prescription of two or more drugs.

Out of the total drugs prescribed 15.3% were fixed dose combinations (FDCs) which was found to be less than that in the studies conducted by Shal et. al. and Johnson et. al. in which the FDCs were reported to be 18% and 24% respectively.<sup>7,9</sup> In the present study the use of FDCs of antihypertensive and antidiabetic drugs is justified as combination of certain drugs that act by different mechanisms is pharmacologically favourable as it has additive therapeutic effects and adverse effects are mutually annulled. For example, tachycardia caused by dihydropyridine calcium channel blockers (e.g. Amlodipine) is counteracted by beta blockers.

In this study 38.5% drugs were prescribed by their brand names and 61.5% of the drugs were prescribed by their generic name. It is comparable to the findings of the study of Solanki et al, which reported the prescription of 74% of the drugs by their generic names.<sup>10</sup> Though, the number of generic drug prescriptions in our study is satisfactory, there is still scope of improvement.

Generic drug prescription is especially important for developing countries like ours as generic substitution substantially decreases cost of therapy. Thus, awareness regarding the same needs to be improved. Widespread use of generic drugs can immensely benefit patients of chronic diseases like Diabetes mellitus and Hypertension. As, these patients are on lifelong therapy, reduction in cost of medicines is helpful for both short term as well as on long term basis.

Out of 600 encounters included in this study, antibiotics were prescribed in 38 (6.3%) encounters which was slightly greater than that found in the study carried out by Hussain et al (4.8%).<sup>6</sup>

Out of total 600 prescriptions, injections were prescribed in only 11.5% of the prescriptions remaining drugs were prescribed by oral route which was similar to the findings of the study conducted by Hussain et. al, in which the injection use was 11.43%.<sup>6</sup> The preference to use of oral

drug therapy was seen in this study which may be due to the ease of administration, availability of drugs and better compliance of patients with regard to oral use of drugs and the study being an outpatient department based study.

The drugs from National Essential List of Medicine (NLEM) and World Health Organisation Model list of Essential Medicine were 52% and 38% respectively, out of 63 different drugs. The prescription from NLEM was found to be lesser in this study in comparison to that reported in the results of the study of Solanki et al. (74.4%).<sup>10</sup> Higher number of drug prescription from these essential lists is an important indicator of safe and effective treatment of common diseases affecting a population and promotion of the rational use of medicines. Thus they help optimize the available health resources of a country.

Unstable Angina, Ischemic Heart Disease and Cerebrovascular Accidents were the most common comorbidities that were present in this study. This may be because of the fact that Diabetes and Hypertension are two leading risk factors which hasten the development of atherosclerosis and as a result lead to the development of Myocardial Infarction and Stroke. Thus, timely management of diabetes and hypertension along with lifestyle changes is advisable.

Cough and Gastric discomfort were the most commonly seen adverse effects in this study. Based on literature and available data it can be stated that cough might be associated with Angiotensin Converting Enzyme Inhibitors and gastric discomfort with Metformin. It was observed that, some adverse drug reactions were mitigated by symptomatic treatment but should also have been evaluated for their cause and treated by dose reduction or prescription of alternative medication. Such ameliorative steps reduce patient's discomfort and improve compliance.

In current study, both NLEM and hospital drug formulary list were available with the hospital dispensary. Out of total 63 different drugs, 25% were from hospital formulary. It is important for the physicians to consult the hospital formulary for safe and cost effective treatment.

#### ***Drug use pattern as per ATC and DDD systems***

##### ***Anatomical Therapeutic Chemical (ATC) classification***

Commonly prescribed drugs (except fixed drug combinations) were classified according to the Anatomical Therapeutic Chemical (ATC) and Daily Defined Dose (DDD) classification. The ATC classification system and the DDD as a measuring unit are recommended by the WHO for drug utilization studies for the ease of representation and comparison of drug utilisation statistics at national, international and other levels and thus improve the quality of research.<sup>11</sup>

A Defined Daily Dose (DDD) is assigned for drugs that already have an ATC code. It is the assumed average

maintenance dose per day for a drug used for its main indication in adults and provide a fixed unit of measurement independent of price, currencies, package size and strength enabling comparisons between population groups.<sup>11</sup>

The prescribed daily dose (PDD) is the average dose that is prescribed in accordance with a representative sample of drug prescriptions.<sup>11</sup> PDD in the current study was found to be significantly less than WHO DDD in all drugs. This difference may be attributed to difference in the area of the patient coverage, sample size of the study, health facility and prescribing attitude of the physicians and awareness of patients regarding the treatment received.

In the present study 568 (95%) prescriptions were in accordance to the JNC VIII guidelines. The patients received thiazide-type diuretic or Angiotensin converting Enzyme Inhibitor or Angiotensin Receptor Blocker or Calcium Channel Blockers, alone or in combination and the patients were seen to be maintained on blood pressure target of <140/90 in patients below 60 years of age and <150/90 in patients sixty or more years. The drug treatment titration strategy was that in case of failure of single drug treatment of Hypertension, second drug was added instead of trying maximum dose of the first medication. All patients in the current study were managed according to the protocol suggested by World Health Organisation for management of diabetes and hypertension. However, the lifestyle changes suggested by the same guidelines such as, smoking cessation, control of glucose and lipid rich diet intake, moderation of alcohol consumption, reduction of sodium intake and moderate to vigorous physical activity, were not observed to be advised to these patients.

The data was collected from the prescription sheets of patients and from the electronic medical databases, thus obviating the chance of Hawthorne's effect which concerns research participation, the consequent awareness of being studied, and possible impact on behavior.<sup>12</sup> In this study the data of drug utilization pattern was studied using internationally accepted parameters such as drug utilization metrics e.g. ATC/DDD classification, PDD and those evolved by WHO. Presentation of data based on internationally accepted parameters helps valid comparison with other such studies. In addition, the compliance of prescribing trends in this study with guidelines of WHO and JNC VIII was also studied.

However, there are certain limitations of the current study. The present study was conducted in a single institute. Studies in different institutes and from different geographical area would cover varied population and could be more appropriate than homogenous population coverage in this study. Also, there was male preponderance in this study. Thus, the results may not be extended to the general population as well as to females with certainty. The study was based on WHO core prescribing indicators which are derived from the data



obtained from the whole world population whereas the population being entirely Indian in this study, substantial differences are seen to be present in the ATC/DDD data.

## CONCLUSION

In conclusion, this study provides an insight into demographic profile, various combinations of drugs prescribed, adverse reactions, comorbid conditions encountered and drug prescription pattern in diabetic hypertensive patients. The data on drug utilisation pattern was fairly comparable to other studies conducted in various parts of India.

This study emphasizes that it is necessary for the physician to be aware of the standard treatment guidelines such as those given by WHO and JNC VIII for the treatment of diabetic hypertensive patients and prescribe the drugs accordingly. Prescribing the drugs according to standard treatment guidelines would mitigate possibility of polypharmacy and the adverse effects associated with the use of multiple drugs and the cost of therapy which may improve compliance of patients. Adherence of the physician to standard treatment guidelines is especially important while treating diseases such as diabetes and hypertension that have a high tendency to accelerate the cardiovascular morbidity and mortality.

Along with pharmacotherapy it is very essential to advice the patients regarding life-style changes which play an adjuvant role, especially in non-communicable, chronic diseases like diabetes and hypertension. This approach may have beneficial effects in control of diabetes and hypertension and subsequently prevent associated cardiovascular complications.

This study highlights the need for improving the prescribing pattern in our setting by adhering more to the WHO model list of essential medicines and by increasing the generic drug prescription. Thus, physicians should be sensitized regarding rational pharmacotherapy; prescribing by generic names and restricting drugs to essential bare minimal in adequate doses and judicious use of antibiotics.

All of these preventive and educational measures along with rational drug prescribing practices would largely help in bringing down the mortality and morbidity associated with hypertension and diabetes in a developing country like ours.

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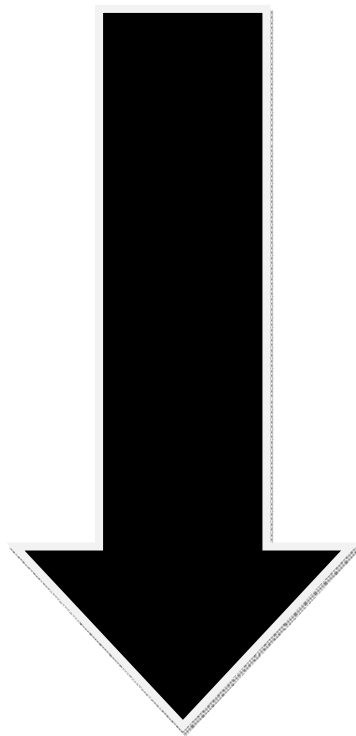
*Ethical approval: The study was approved by the Institutional Ethics Committee*

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# Pharmacology Publications 2019



**Study of drug prescription pattern in ischemic heart disease patients****Mahadeo P. Sawant, Sudhir L. Padwal\*, Rakesh R. Jadhav, Harshal N. Pise, Rucha Shinde**

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**ABSTRACT**

**Background:** Drug utilization pattern studies helps to screen, assess and propose appropriate modifications in prescription practices, this would help to make patient care rational and cost effective. Study was intended to analyse the drug prescribing pattern for treatment of Ischemic heart disease using WHO indicators.

**Methods:** This is a cross sectional observational study conducted on ischemic heart disease patients admitted at inpatient department of medicine in a tertiary care teaching hospital. The study consisted of analysis of drug utilization pattern of prescribed drugs.

**Results:** IHD was more commonly seen in males (70.06%) than females (29.94%). IHD was most commonly seen in patients of age group of 61-70 year. Drugs prescribed to patients belong to various therapeutic classes ranging from anti-platelets, anticoagulants, anti-anginal, antithrombin, thrombolytic, hypolipidemics. The most commonly prescribed therapeutic class of drugs was antiplatelet (86.26%) followed by hypolipidemic (82.25%) and ACE inhibitors drugs (46.60%). Average number of drugs per encounter was 7.70. Drugs were prescribed by their generic names were 29.99%. Out of total study group 22.06% patients were prescribed at least one antibiotic. Injections were prescribed only in 1392 (27.86%) out of 4995 drugs. Of total drugs 3270 (65.45%) of drugs were from National List of Essential Medicines-2016 (NLEM -2016) and 2774 (55.53%) drugs prescribed were from WHO-EML-2016.

**Conclusions:** Risk of artery disease increased with increasing age. IHD was more common in males than females. The most commonly prescribed drug classes in Ischemic heart disease were anti-platelet drugs followed by hypolipidemic agents.

**Keywords:** Anticoagulants, Antiplatelet, ACE inhibitors, Drug utilization, Hypolipidemics, Ischemic heart disease

**INTRODUCTION**

Ischemic heart disease (IHD) is a condition in which there is an inadequate supply of blood and oxygen to a portion of the myocardium, it occurs if there is imbalance between myocardial oxygen supply and demand. The common cause of myocardial ischemia is atherosclerosis of epicardial coronary artery/arteries which leads to regional reduction in myocardial blood flow and inadequate perfusion of the myocardium supplied by the involved coronary artery.<sup>1</sup>

Ischemic heart disease (IHD) is one of the leading causes of mortality and it is also a primary cause of premature mortality and disability in developing countries like India.<sup>2</sup> Noncommunicable diseases (NCDs) kill 40 million people each year, equivalent to 70% of all deaths globally. Each year, 17 million people die from a NCD before the age of seventy, and 87 percentages of premature deaths occur in low and middle-income countries. Cardiovascular diseases account for most non-communicable diseases deaths, (17.7 million population yearly) which is followed by cancers (8.8 million), respiratory diseases (3.9 million), and diabetes (1.6 million).<sup>3</sup>



The World Health Organization (WHO) and Global Burden of Disease Study also have highlighted increasing trends in years of life lost (YLLs) and disability-adjusted life years (DALYs) from IHD in India. In India, studies have reported increasing IHD prevalence over the last 60 years, from 1% to 9%-10% in urban populations.<sup>4</sup> Striking features of IHD epidemiology in India are high mortality rates, premature CHD, and increasing burden.<sup>5</sup> Among the causes for this rising burden, the upcoming pandemic of obesity and diabetes further enhances the estimates of CV mortality and healthcare costs over the next decades.

Despite the stress on primary prevention, CV risk factors are still poorly. In chronic conditions such as hypertension, ischemic heart disease (IHD) and cardiac failure, the progressive use of multiple drugs is common. Polypharmacy is associated with an increased morbidity with increasing in the costs. Prescribing multiple drugs often leads to inappropriate utilization of drugs, lower adherence to treatment and increase in chances of side effects.

The risk factors for ischemic heart disease include dyslipidemia (high apolipo-protein B / apolipo-protein A1 ratio), tobacco use, smoking, hypertensive and/or diabetic patients, obese, physical sedentariness, lowfruits and vegetable intake, and stress.<sup>6</sup> Drugs play important role in promoting health of patients who are seeking treatment for various ailments, however to get these desired effects drugs should be safe and efficacious. Drugs must be utilized judiciously.

Drug utilization pattern studies helps to screen, assess and propose appropriate modifications in prescription practices; this would help to make patient care rational and cost effective. Rational drug prescribing is defined patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community.<sup>7</sup>

Drug utilization studies are influential aid to ascertain the role of drug in the society. The World Health Organization (WHO) has defined drug utilization research as the marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences.<sup>8</sup> Drug therapy is available often at an unaffordable price. Hence, it is very important to realize that dispensing inappropriate and irrational drugs for treatment of various disease leads to potential hazards.<sup>9</sup> It is globally a major concern. So it is very important to review the drug utilization pattern periodically, to ensure its safety and efficacy.<sup>10</sup>

World Health Organization (WHO) and International Network of Rational Use of Drugs (INRUD) have provided guidelines of rational drug use. When applied, these indicators give fair idea about prescription pattern, availability of drugs and patients comprehension about therapy. It helps to overcome the shortcoming and enhance

the performance from day to day.<sup>11</sup> Indiscriminate use of drugs in ischemic heart disease patient may lead increased adverse events. Still, very scanty data is available regarding drug utilization pattern in Ischemic heart disease treatment. In the given circumstances, present study is proposed to investigate prescription and drug utilization practices in ischemic heart disease patients admitted in Medicine ward in a government tertiary care hospital in Maharashtra.

## METHODS

### *Methodology*

This is a cross sectional observational study conducted on ischemic heart disease patients admitted at inpatient department of Medicine in a tertiary care teaching hospital.

The study consisted of analysis of drug utilization pattern of prescribed drugs.

### *Study population*

All ischemic heart disease patients admitted in medicine inpatient department were enrolled in the study as per the following inclusion and exclusion criteria over a period of January 2016-June 2017.

### *Inclusion criteria*

All diagnosed cases of in-patients with ischemic heart disease during the study period (January 2016- June 2017).

### *Exclusion criteria*

- Patient not willing to consent for the study
- Outpatients Department (OPD) patients
- Patients who were under day care management

### *Statistical analysis*

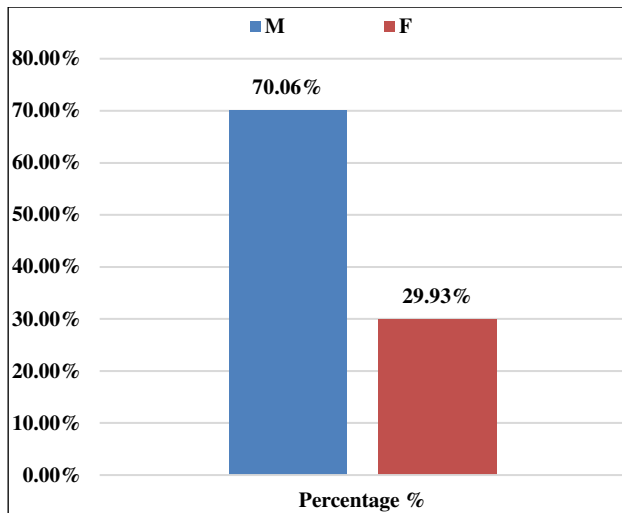
The statistical analysis was done with the help of Microsoft Excel 2010 software.

## RESULTS

### *Demographic data*

Around 648 patient's data, who were admitted during Jan-2016 to June 2017, was collected and analyzed. The demographic data is shown in Figure 1 as follows.

IHD was more commonly seen in males (70.06%) than females (29.94%). IHD group patients were divided according to age in 7 classes. As per study analysis, IHD was most commonly seen in patients of age group of 61-70 year. The mean age of study group was 65.32 Years. (Age wise details are as shown in (Table 1).



**Figure 1: Gender wise distribution of patients**

**Table 1: Age group wise distribution of patients.**

| Age group   | Number | Percentage (%) |
|-------------|--------|----------------|
| 20-30 Yrs   | 9      | 1.38 %         |
| > 30-40 Yrs | 21     | 3.24 %         |
| >40-50 Yrs  | 76     | 11.72 %        |
| >50-60 Yrs  | 124    | 19.13 %        |
| > 60-70Yrs  | 278    | 42.90 %        |
| >70-80 Yrs  | 108    | 16.66 %        |
| >80 Yrs     | 32     | 4.93 %         |

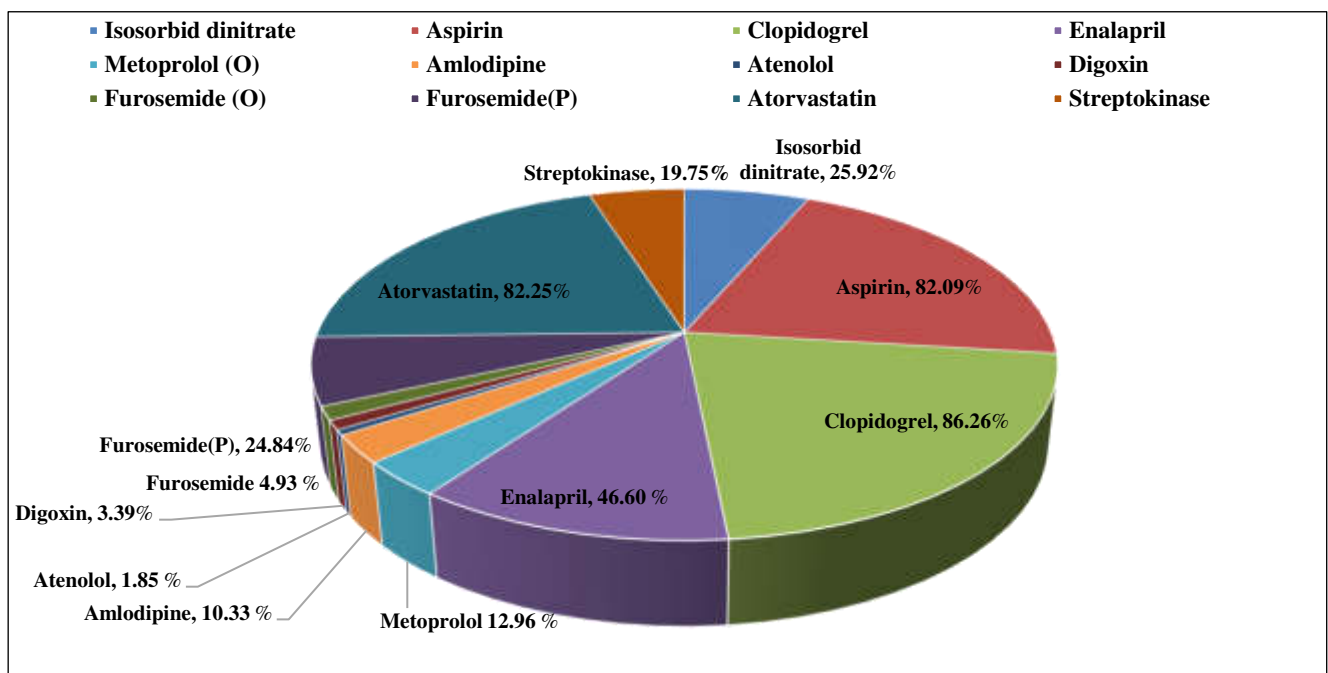
Total 4995 drugs were prescribed to 648 patients of Ischemic heart disease during our study. The number of

drugs ranged from 4-14 per patient with average of 7.70 drugs per patient. (Table 2).

**Table 2: Number of drugs prescribed per prescription.**

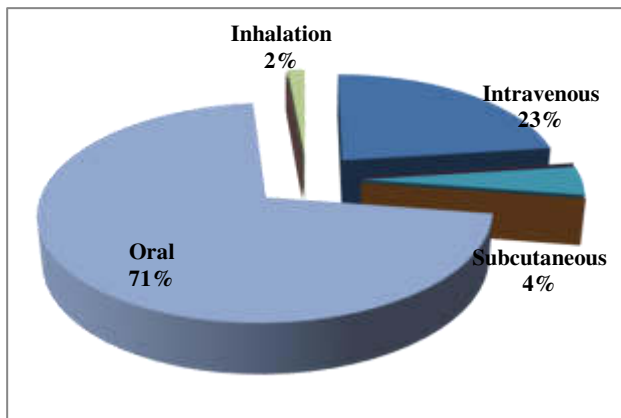
| No. of drugs | No. of prescriptions | Percentage (%) |
|--------------|----------------------|----------------|
| 4            | 13                   | 2.00 %         |
| 5            | 42                   | 6.49 %         |
| 6            | 67                   | 10.35 %        |
| 7            | 145                  | 22.41 %        |
| 8            | 167                  | 25.81 %        |
| 9            | 106                  | 16.38 %        |
| 10           | 79                   | 12.21 %        |
| 11           | 25                   | 3.86 %         |
| 12           | 2                    | 0.30 %         |
| 14           | 1                    | 0.15%          |

Drugs prescribed to patients belong to various therapeutic classes ranging from anti-platelets, anticoagulants, anti-anginal, antithrombin, thrombolytic, hypolipidemics. The most commonly prescribed therapeutic class of drugs was anti-platelet (86.26%) followed by hypolipidemic (82.25%) and ACE inhibitors drugs (46.60%). Mostly commonly prescribed drug was clopidogrel (86.26%) followed by atorvastatin (82.5%), aspirin (82.09%), enalapril (46.60%), asosorbide dinitrate 25.92%, furosemide (P) 20.84%, metoprolol 12.96%, Amlodipine 10.33%, Furosemide 4.93%, digoxin 3.3%, atenolol 1.85%. (Figure 2).



**Figure 2: Percentage of drugs prescribed as per drug class.**

Out of total 4995 of drugs prescribed, maximum drugs 71.19% were prescribed in oral formulations. (Figure 3) followed by intravenous (22.95%) and subcutaneous (4%), as shown in Figure 3.



**Figure 3: Various routes of drug administration WHO core drug use indicators.**

#### Prescribing indicators

- Average number of drugs per encounter
- Total of 4994 drugs were prescribed to 648 patients. So, average number of drugs per encounter was 7.70. Out of total 4995 of drugs prescribed, maximum drugs 71.19 % were prescribed in oral formulations
- Percentage of drugs prescribed by generic names
- In previous studies reviewed, prescribing drugs with brand names was commonly observed practice. In current study prescription analysis showed that 1498 (29.99%) drugs were prescribed by their generic names
- Percentage of encounters with antibiotics prescribed:
- In present study, antibiotics were prescribed to few patients. Out of 648 prescriptions, 143 (22.06%) were having at least one antibiotic
- Percentage of encounters with injections prescribed  
Injections were prescribed only in 1004 (26.89%) out of 4995 drugs
- Percentage of drugs prescribed from essential drug list or formulary
- Of total drugs 3270 (65.45%) of drugs were from National List of Essential Medicines -2016 (NLEM - 2016) and 2774 (55.53%) drugs prescribed were from WHO-EML-2016

## DISCUSSION

Drug utilization studies are useful to determine the behavior of the use of medicines in a society.<sup>12</sup> Since past few years many research drug utilization studies are being performed worldwide to assess and to understand the safe and more effective drug utilization, these studies are indicating that irrational drug use is a universal phenomenon. Countries like India are becoming global epicenter for various diseases like ischemic heart disease

and diabetes. Hence, it is the need of the time to decrease the risk factors and to improve the treatment strategies for these diseases.<sup>12</sup>

Around 648 patient's prescriptions were analyzed from medicine ward for 18 months. Study results indicated that male (70.06%) patients had a high frequency of ischemic heart disease incidences as compared to female (29.94%) patients which were in accordance to Nagabushan H. et al, and Sreedevi K et al.<sup>13,14</sup> As per Dawalji S et al, 72.94% patients were male and 27.06% were female as per other study by Tamilselvan T et al, 69.1% accounts for males and 30.8% accounts for females as per Sreedevi K et al, gender-wise distribution showed males 61.5% predominance, whereas, females were 38.5%.<sup>14,15,16</sup> Whereas, similar study by Shankar R et al, showed the female (51.94%) predominance over males (48.06%).<sup>17</sup> The study results were found to be consistence with most of the previous studies and indicated that male are more prone to coronary artery disease as compared to female.

#### WHO core drug use indicators

##### Average number of drugs per prescription

In current study, the number of drugs prescribed ranged from four to fourteen per patient. So, average number of drugs per prescription was 7.70. It is comparable to the average number of drugs prescribed in the studies of Nagabushan H et al, (7.8).<sup>13</sup> It is much less as compared to the findings of Sandozi T et al, (9.93) and little higher than Shankar R et al, 3.39 drugs per patients.<sup>17,18</sup>

This difference can be due to variation in drug prescription habits and patient need and sometimes choice of patients.

##### Percentage of drug prescribed by generic names

In this study, data analysis showed that 1498 (29.99%) drugs were prescribed by with generic names. In study by Nagabushan H et al, drugs prescribed by their generic names were 52.9% which is higher than present study while in the study of Sandozi T et al, were 6%.<sup>13,19</sup> This is much less as compared to present study. Similar findings were reported in study Shankar R et al, (36.43%).<sup>17</sup> A prescription could be considered as appropriate if prescribed in the form of generic drugs. This would help in reducing the cost of treatment for the patients. It also helps in decrease prescription writing errors and confusion in dispensing of different brand names which sound alike and/or spell similar.

##### Percentage of encounters with antibiotics

In present study, antibiotic is one of the prescribed therapeutic classes of drugs. Out of 648 prescriptions, 143 (22.06%) were having at least one antibiotic. This finding is much lower than the similar studies by, Christain RP et al, 37.9%, Nagabushan H et al, 40.20%, Dawalji S et al, 92.94%, and higher than the study by Tamilselvan T et al,



16 3.20%.<sup>13,15,16,19</sup> This is in accordance to WHO recommendation for use of minimum required antibiotics, which helps to decrease the polypharmacy, decrease chances of developing resistance, and adverse drug reactions

#### *Percentage of encounters with injections*

In this study, injections were prescribed only in 1392 (27.86%) out of 4995 drugs. In a similar study of Nagabushan H et al, 100% drugs were given by injections.<sup>13</sup> These findings are in contrast with those of studies of Shankar R et al, were injectable preparations used for only 7.89% of drugs.<sup>17</sup> Lower usage of injectable drugs is in accordance WHO recommendations as oral route is safer than injections.

#### *Percentage of drugs prescribed from National List of Essential Medicines (NLEM)*

In this study, out of total 4995 drugs, 3270 (65.45%) of drugs were from National List of Essential Medicines (NLEM) and 2774 (55.53%) drugs prescribed were from World Health Organization Essential Medicines List (WHO-EML). Some other similar studies cited in the literature e.g. Nagabushan H et al, 75.1% and Shankar R et al, 60.32% drugs were prescribed from WHO-EML.<sup>13,17</sup> Higher percentage of prescribed drugs from NLEM may be indicative of rational prescribing. Adherence to NLEM for drug prescription not only promotes the rational use of medicines but also optimize the available health resources of a country.

This study had few limitations. It was conducted at a single tertiary healthcare centre. Studies with data from multi-centric group of population in similar context would give additional information on this aspect. This study population was relatively homogenous. Hence, this study results may not be generalized to other population. It was a quantitative type of drug prescribing pattern study with the WHO core prescribing indicators and therefore determining the quality of diagnosis and the appropriateness of treatment was beyond scope of prescribing indicators.

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*Ethical approval: The study was approved by the Institutional Ethics Committee*

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# A comparative study of functional outcome of dynamic compression plating versus interlocking nailing for fracture shaft to humerus at tertiary health care center

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## Abstract

**Background:** Most diaphyseal fractures can be managed conservatively and good results achieved in most cases. **Aims and Objective:** To Study Functional Outcome Of Dynamic Compression Plating Versus Interlocking Nailing For Fracture Shaft To Humerus At Tertiary Health Care Center. **Methodology:** This was a cross-sectional study carried out in the patients presented with Fracture Shaft To Humerus during the one year period i.e. June 2018 to June 2019 in the one year period there were 50 patients enrolled to study by written and explained consent 25 were given surgical treatment by Dynamic Compression Plating (DCP, n=25) and remaining 25 by Interlocking Intra-medullary Nailing (IMN, n=25). The statistical analysis was done by Chi-square test, unpaired t-test and calculated by SPSS 19 version software. **Result :** In our study we have seen the average age in both the group was comparable i.e. 45.23 ± 3.42 Yrs. and 44.56 ± 4.39 (p>0.05, t=0.82, df=49) and Male to Female ratio was also comparable i.e. 1.5 : 1 and 1.08:1 (p>0.05, X<sup>2</sup>=0.25, df=1). The most common complication were Impingement 12% Vs 20%; Shoulder stiff 8% Vs 12%; Stiff Elbow 8% Vs 12%; Infection 8% Vs 8% and overall the complications were comparable respectively in DCP and IMN groups (X<sup>2</sup>=1.662, df=7, p>0.05). Overall Excellent results were 68% Vs 40%, Moderate 28% Vs 32%; Poor 4% Vs 28% respectively in DCP and IMN Group (X<sup>2</sup>=6.38, df=2, p<0.04). **Conclusion:** It can be concluded from our study that Functional Outcome of DCP were superior as compared to Intra medullary Nails with respect to excellent outcome where as complications were comparable in both the groups.

**Key Words:** Dynamic Compression Plating, Interlocking Nailing, Fracture Humerus.

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## INTRODUCTION

Most diaphyseal fractures can be managed conservatively and good results achieved in most cases.<sup>1</sup> However loss

of reduction in the plaster cast invariably leads to malunion. Operative treatment for humerus fractures has usually been reserved for cases of delayed union, non-union, or malunion following conservative management.<sup>1</sup> The advantage of operative management is early mobilization and patients comfort. Surgical stabilization can be accomplished with different implants and techniques; the most common are open reduction with plate fixation or stabilization with intramedullary nails. Both techniques have certain mechanical and anatomical advantages and disadvantages. <sup>1</sup> Plating gives good results but disadvantages that it requires extensive dissection and radial nerve protection.<sup>2</sup> The plate may fail in osteoporotic bone hence locking plate is advisable. With the dynamic success of intramedullary fixation of

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fractures of the femur and tibia, there was speculation that this technique might be more appropriate for humerus shaft fracture than plating.<sup>1</sup> Intramedullary nails have the advantage of closed insertion techniques, intact periosteal blood supply, and load-sharing mechanical properties.<sup>1</sup> But unfortunately the success of interlocking nailing in long bones of lower limbs is not seen in humerus hence we have done study to see the outcome of two treatment methods for the fracture of humerus at tertiary health care centre

## METHODOLOGY

This was a cross-sectional study carried out in the patients presented with Fracture Shaft To Humerus during the one year period i.e. June 2018 to June 2019 in the one year period there were 50 patients enrolled to study by written and explained consent 25 were given surgical treatment by Dynamic Compression Plating (DCP ,n=25) and remaining 25 by Interlocking Intra-medullary Nailing(IMN,n=25) . All details of the patients like age, sex and complications if any and out come was assessed by Rommens *et al* Series grading\* Into Excellent, Moderate ,Poor . The statistical analysis was done by Chi-square test, unpaired t-test and calculated by SPSS 19 version software.

## RESULT

**Table 1:** Distribution of the patients as per the age and sex

|        | DCP (n=25)  | ILN (n=25)  | p-value                           |
|--------|-------------|-------------|-----------------------------------|
| Age    | 45.23 ±3.42 | 44.56± 4.39 | p>0.05,t=0.82,df=49               |
| Sex    |             |             |                                   |
| Male   | 15          | 13          | p>0.05, X <sup>2</sup> =0.25,df=1 |
| Female | 10          | 12          |                                   |

The average age in both the group was comparable i.e. 45.23 ±3.42 Yrs. and 44.56± 4.39 (p>0.05,t=0.82,df=49) and Male to Female ratio was also comparable i.e. 1.5 : 1 and 1.08:1(p>0.05, X<sup>2</sup>=0.25,df=1)

**Table 2:** Distribution of the patients as per the complications

| Complications     | DCP (n=25) | IMN (n=25) |
|-------------------|------------|------------|
| None              | 12(48)     | 9(36)      |
| Impingement       | 3(12)      | 5(20)      |
| Shoulder stiff    | 2(8)       | 3(12)      |
| Stiff Elbow       | 2(8)       | 3(12)      |
| Infection         | 2(8)       | 2(8)       |
| Open reduction    | 2(8)       | 1(4)       |
| Splintering of DF | 1(4)       | 1(4)       |
| Non-union         | 1(4)       | 1(4)       |
| Wrist drop        | 25(100)    | 25(100)    |

(X<sup>2</sup>=1.662,df=7,p>0.05)

The most common complication were Impingement 12% Vs 20%; Shoulder stiff 8% Vs 12%; Stiff Elbow 8% Vs 12%; Infection 8% Vs 8% and overall the complications

were comparable respectively in DCP and IMN groups (X<sup>2</sup>=1.662,df=7,p>0.05)

**Table 3:** Distribution of the patients as per the outcome of treatment

| Outcome   | DCP (n=25) | IMN (n=25) |
|-----------|------------|------------|
| Excellent | 17(68)     | 10(40)     |
| Moderate  | 7(28)      | 8(32)      |
| Poor      | 1(4)       | 7(28)      |

(X<sup>2</sup>=6.38,df=2,p<0.04)

Overall Excellent results were 68% Vs 40%, Moderate 28% Vs 32%; Poor 4% Vs 28% respectively in DCP and IMN Group (X<sup>2</sup>=6.38,df=2,p<0.04) .

## DISCUSSION

Incidence of Shaft Of Humerus Fractures Is 1% To 3% Of All Fractures <sup>3-5</sup> In The Human Body And 20% Of All Fractures Of Humerus <sup>6</sup>. The Common Causes Of Shaft Of Humerus Fractures In The Elderly Patients Are Simple Falls Or Rotational Injuries. In Younger Population, The Causes Are High Energy Trauma Like Road Traffic Accident And Fall From Height. There Are So Many Treatment Modalities For Shaft Of Humerus Fracture Depending On The Age Of The Patient, Fracture Pattern, Soft Tissue Condition, Bone Quality And Associated Complications Of The Patient. Treatment Options Include Conservative and Operative Treatment. Conservative Methods Include U Slab, Hanging Cast, Sling And Body Bandage, Velpeau Bandage And Functional Bracing <sup>7</sup>. Most Of The Shaft Of Humerus Fracture Cases Can Be Treated Conservatively With Good Results. However There Are Certain Cases Which Are Best Treated With Operative Techniques. Indications For Operative Treatment Are Open Fracture, Non-Union, Malunion, Failure After Conservative Treatment, Polytrauma Patient, Fractures Associated With Neurovascular Impairment Or Intra Articular Extension.<sup>8</sup> Operative Treatment Include Plate And Screws, Intramedullary Nail. Intramedullary Nails Can Be Inserted Either By Antegrade Or Retrograde Manner. Intramedullary Nailing Has The Disadvantages Of Rotator Cuff Injuries, Joint Stiffness And Joint Morbidity. Open Reduction And Internal Fixation (ORIF) Has The Advantages Of Good Reduction, Stable Fixation, Rotational Stability And Early Mobilization Most surgeons agree that intramedullary nailing is not best fixation for humerus shaft as compare to tibia and femur shaft fracture. Plate osteosynthesis requires extensive soft tissue dissection with the risk of radial nerve damage<sup>5</sup> and infection. The indication s for open reduction and internal fixation of acute fractures of the humeral shaft have been described as open fractures, fractures associated with vascular or neural injuries or with lesions of the shoulder, elbow or forearm in the same limb; bilateral upper extremity

injuries, fractures for which closed methods of treatment have failed and pathological fractures, fractures in patients with multiple injuries.<sup>9,10,12,13</sup> In our study we have seen the average age in both the group was comparable i.e. 45.23  $\pm$  3.42 Yrs. and 44.56  $\pm$  4.39 ( $p > 0.05$ ,  $t = 0.82$ ,  $df = 49$ ) and Male to Female ratio was also comparable i.e. 1.5 : 1 and 1.08:1 ( $p > 0.05$ ,  $X^2 = 0.25$ ,  $df = 1$ ) The most common complication were Impingement 12% Vs 20%; Shoulder stiff 8% Vs 12%; Stiff Elbow 8% Vs 12%; Infection 8% Vs 8% and overall the complications were comparable respectively in DCP and IMN groups ( $X^2 = 1.662$ ,  $df = 7$ ,  $p > 0.05$ ) Overall Excellent results were 68% Vs 40%, Moderate 28% Vs 32%; Poor 4% Vs 28% respectively in DCP and IMN Group this observed difference was statistically significant ( $X^2 = 6.38$ ,  $df = 2$ ,  $p < 0.04$ ) These findings are similar to Yash B. Rabari<sup>14</sup> they found that Dynamic compression plating is preferable technique than interlocking nailing for fracture shaft of humerus in adults.

## CONCLUSION

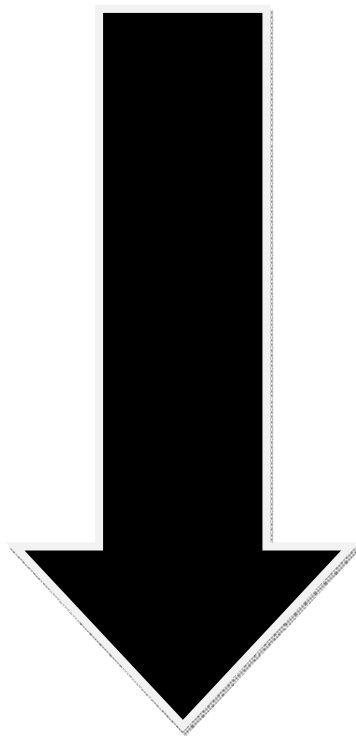
It can be concluded be concluded from our study that Functional Outcome of DCP were superior as compared to Intra medullary Nails with respect to excellent outcome where as complications were comparable in both the groups.

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# Pharmacology Publications 2019





**Study of adverse drug reactions in a tertiary care hospital****Santosh B. Godbharle, Sudhir L. Padwal\***

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**ABSTRACT**

**Background:** The objectives of the study were to evaluate incidence and preventability of adverse drug events (ADEs) and potential ADEs and to analyse preventable events to develop prevention strategies.

**Methods:** The study was retrospective observational study conducted at a rural tertiary care hospital at Maharashtra, for 12 months. Patients of both gender and all age group were included in the study. These entire adverse drug reactions were reported either by the PVPI assistance and/or hospital staff and their severity and causality assessments was performed as per Naranjo's and Hartwig's assessment criteria respectively. Data was analyzed by using Microsoft Excel.

**Results:** There were total 256 ADR (adverse drug reactions) were reported in 12 months from January 2018 to December 2018 in various departments of the study center. Most of the adverse drug reactions were reported among age group of 21–40 years patients. Rash and itching (69) were most commonly reported ADR's. ART (31.25%), antibiotics (28.90%) were reported to induce maximum number of ADRs. Most of the adverse drug reactions were possible (194, 75.78%) and mild (208, 81.25%) in nature.

**Conclusions:** The antibiotics, ART drugs were most common drugs to reported ADRs. The commonly reported reactions were rash and itching.

**Keywords:** Adverse drug reaction, Pharmacovigilance, Causality assessment, Naranjo's, Hartwig's assessment, Antibiotics ADR

**INTRODUCTION**

Though the drugs are prescribed for the desirable therapeutic effects, but they are not devoid of adverse effects/ side effects and hence drugs should be judiciously prescribed considering their likely unwanted harmful effects. An adverse drug reaction (ADR) is defined by the World Health Organization (WHO) as any noxious, unintended, or undesired effect of a drug that occurs at doses used in humans for prophylaxis, diagnosis, or therapy.<sup>1</sup> Adverse drug reactions take place nearly day-to-day in health care institutions and can affect patient's quality of life, often causing considerable morbidity and sometimes even mortality.<sup>2</sup>

Pharmacovigilance activity has been introduced to monitor and analyses any such unwanted effects of drugs. As per WHO, Pharmacovigilance (PV) is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem. Adverse drug reaction (ADR) are common in the patients who are suffering from severe and complex disease process or are on multiple drugs, leading to possibility of drug-drug interactions.

Multiple factors influence ADR susceptibility, including multiple drug therapy, disease severity, age, and the type and number of drugs prescribed.<sup>3</sup> Hence attention has been given to recognizing the patient population at risk,

the drugs most frequently responsible, and the likely causes of ADRs. An upsurge in the number of drugs on the market, an aging population, and an upward trend in polypharmacy are contributing factors to the incidence and prevalence of ADRs worldwide. Adverse drug reactions may lead to loss of belief in or have undesirable feelings toward their doctors and may lead to pursue self-medication, which may thus increase further ADRs. Around 5% of all hospital admissions are the result of an ADR, and around 10%–20% of inpatients will have at least one ADR during their hospital stay.<sup>4</sup> The actual incidence of ADRs may be even greater because some ADRs mimic natural disease states and may thus go undetected and/or unreported. Although some ADRs present as minor symptoms, others are serious and cause death in as many as 0.1%–0.3% of hospitalized patients.<sup>5</sup> Adverse drug reactions should be quickly identified and managed to limit their detrimental effects on the patient. The cost of managing ADRs can be high, whether they occur in the inpatient or the outpatient setting. Because the clinical diagnosis of an ADR is not always obvious, practitioners often order additional laboratory tests or procedures to investigate the cause of a patient's sufferings.<sup>5</sup>

Since drugs are intended to relieve suffering, patients find it particularly offensive that they can also cause disease. It has been reported that ADRs account for 5% of all hospital admissions and occur in 10–20% of hospitalized patients.<sup>6</sup> An overall incidence of serious and fatal ADR among hospitalized patients is 6.7% and 0.32%, respectively. Sometimes, ADR-related costs, such as hospitalization, surgery and lost productivity, exceed the cost of the medications.<sup>4</sup> The recent epidemiological studies have estimated that adverse drug reactions are the fourth to sixth leading causes of death.<sup>7</sup> Moreover, detection of ADRs has become increasingly significant because of introduction of a large number of potent toxic chemicals as drug in last two or three decades. Thus, it became very crucial to monitor both known and unknown adverse effects of medicines.

Though ADRs are of great concern to the general public, medical profession, pharmaceutical industry and regulatory authorities, the concept of ADR reporting is still new in India and reporting of ADRs is infrequent. Govt. of India under the guidance of Ministry of Health and Family Welfare has initiated an ADR reporting program known as Pharmacovigilance Program of India and has established adverse drug reaction monitoring centers in various tertiary care hospitals across the country to monitor ADRs.<sup>8</sup> However, from this region still there is underreporting of ADRs. Hence, this study was undertaken to record and analyze adverse drug reactions reported from various departments of a tertiary care hospital situated at Rural Medical College, Maharashtra. We have also analyzed ADRs for causality and severity.

## METHODS

An observational, cross-sectional study was carried out for 12 months from January 2018 to December 2018 at a Rural Medical college and Hospital in Maharashtra, India. ADRs were reported from outpatient departments as well as from wards of cardiology, dermatology, gynaecology, medicine, ophthalmology, paediatric, psychiatry, TB and chest, and neurology department of the hospital. Those cases which were identified and reported by physicians of this hospital were considered as an ADR and recorded. The collected information included patient's initial, age, gender, reporting department of the hospital, description of the reaction, duration of reaction, name of the suspected drug causing reaction, and outcomes. Drugs causality assessment was performed by Naranjo's probability assessment scale and Hartwig's criterion was used for severity assessment.<sup>9,10</sup> Attempt of Rechallenge was not found in any patient. Outcome of the patients with ADR were recorded as fatal, fully recovered (patient fully recovered during study period), recovering (patient recovering, but not fully recovered during study period) and unknown (insufficient information and not documented).

### Inclusion criteria

All the suspected ADRs that may be due to the medications, both prescribed and over the counter, taken by patients either as inpatients or outpatients, that were ultimately noted.

### Exclusion criteria

The use of alternative system of medicines such as Ayurveda, Homeopathy, Unani, etc. as well as over prescribing, over dosage, excess consumption and patients taking more than ten prescription drugs were excluded. All mentally retarded, drug addicted, and unconscious patients were also excluded from the study. Patients admitted due to alcohol or drug abuse, a suicide attempt or admissions planned more than 24 h in advance were not recorded. Naranjo ADR probability scale for causality assessment.

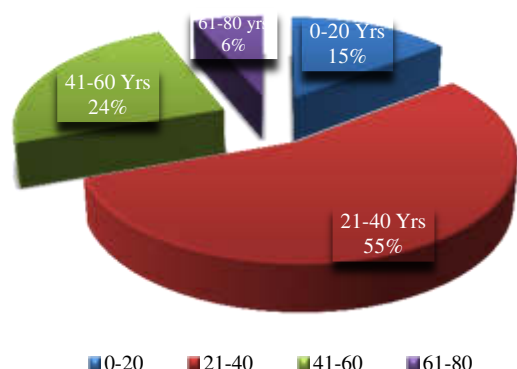
### Statistical analysis

Description statistics were used for data analysis with the help of Microsoft Excel.

## RESULTS

In this study, 256 patients were reported to experience ADR during study period. Most of the patients (52.37%) were reported from in-patient departments and rests (47.63%) were reported from outpatient department of the hospital. The mean age of the patients was 35.56 years; youngest patient was of 1 year 6 months and oldest being 81 years. Majority of the patients (55.07%) experienced ADRs belonged to age group of 21–40 years (Figure 1).

Out of 256 patients, 122 (47.64%) patients were male while 134 (52.36%) patients were female as shown in Table 1.



**Figure 1: Age distribution of patients with ADRs.**

**Table.1 Gender distribution in study population.**

| Gender | Number | Percentage (%) |
|--------|--------|----------------|
| Male   | 122    | 47.65          |
| Female | 134    | 52.34          |

**Table 2: Types of ADRs.**

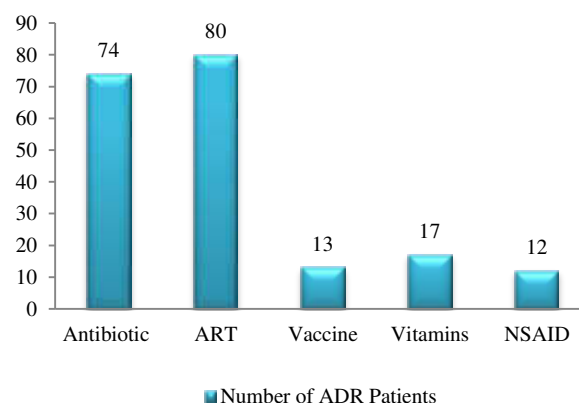
|                                       | Number | Percentage (%) |
|---------------------------------------|--------|----------------|
| Skin rash/ Itching / Hypersensitivity | 69     | 34.37          |
| Swelling (local area)                 | 18     | 7.03           |
| Anemia                                | 17     | 6.64           |
| Diarrhea                              | 16     | 6.25           |
| Fever                                 | 7      | 2.73           |
| Dizziness                             | 6      | 2.34           |
| Steven Jonson syndrome                | 2      | 0.78           |
| Breathlessness                        | 2      | 0.78           |
| Others                                | 100    | 39.06          |

In this study, 256 ADRs were reported from various departments of the hospital. Of all reported ADRs, most common ADR was rash and itching / Hypersensitivity (34.37%) and followed by local swelling (7.03%). (Table. 2) The antibiotics and antiretroviral (ART) was most common drugs reported to causing ADRs, as shown in Figure 2. Skin was the most commonly affected organ system (54.32%).

**Table 3: Causality assessment of ADRs.**

| Types    | Number | Percentage (%) |
|----------|--------|----------------|
| Probable | 194    | 75.78          |
| Possible | 28     | 10.93          |
| Definite | 32     | 12.50          |

According to the Naranjo's algorithm scale, 194 (75.78%) assumed ADRs were probable, 28 (10.93%) ADRs were reported as possible and 32 (12.50%) ADRs were reported as definite (Table 3). According to Hartwig severity assessment scale, most of the ADRs were mild 208 (81.25%), moderate 26 (10.15%) and 20 (7.81%) ADR report was severe (Table 4). Most of the patients with ADRs 251 (98.04%) were completely recovered after treatment and 5 (1.96%) ADRs had lost to follow up hence their outcome was unknown.



**Figure 2: Class of drugs causing ADRs.**

**Table 4: Severity assessment of ADRs.**

| Severity | Number | Percentage (%) |
|----------|--------|----------------|
| Severe   | 20     | 7.81           |
| Moderate | 26     | 10.15          |
| Mild     | 208    | 81.25          |

## DISCUSSION

In this study, 256 ADRs were reported during study period. Most commonly it occurred in age group of 21-40 years. Though, elderly patients are more prone to ADRs but in this study ADRs were reported in younger age group as it is likely that this population was attending hospital more frequently to study center. Elderly predisposes to ADRs due to changed pharmacokinetics and pharmacodynamics, co-morbidity from chronic diseases, disease burden, severity of illness, polypharmacy and use of inappropriate drugs.<sup>11</sup> It has been observed in this study that ADRs were more common in females as compared to males. Majority of ADRs were reported from female patients than from male. The female gender was associated with higher risk of ADRs than male.<sup>12,13</sup> Similar results have been reported by Singh et al were 67.67% of study population of ADRs was females.<sup>14</sup>

But as per previous study by Priyadharsini et al and Mandavi et al, ADRs are most commonly seen in Pediatric and geriatric group of patients as they are susceptible groups for ADR more frequently. But the result of our study does not match with these studies.<sup>15,16</sup>



Most of the ADRs were reported from Medicine department and ART center this might be due to the increasing awareness among physicians regarding ADR reporting. Similar kind of results were reported from previous study Shamna et al and Lihite et al.<sup>17,8</sup>

In this study, rash and itching, hypersensitivity reaction, local swelling, anemia, diarrhea were commonly reported ADRs. Steven Jonson syndrome (SJS) is rare but potentially life threatening serious ADR which was also reported in our study, although in two patients but as it life threatening reaction patients were treated accordingly on priority basis with final outcome of complete recovery and no mortality.

In our study, majority of the ADRs were associated with ART drugs and antibiotics drugs. Similar results were obtained by study done by Singh et al and Laskar et al were antibiotics commonly associated with adverse drug reaction.<sup>14,18</sup> As per analysis of data obtained most of reported ADRs were probable 75.78%, followed by definite 12.50% and possible was 10.93%. As per Hartwig criteria most of the ADR reports were mild in nature and recovered during study period. These findings are similar to the previous studies done by Arulmani et al and Shrivastava et al.<sup>19,20</sup>

### Limitations

This study suffers the main drawback of spontaneous reporting system i.e. underreporting. Thus, ADR monitoring should be strengthened in this diversified region by sensitizing and encouraging healthcare providers to report ADRs.

### CONCLUSION

The Antimicrobials, antibiotics and ART drugs were reported to cause majority of ADRs in this tertiary care center. The commonly reported ADR in this study was rash and itching. This study suggests that there is a need of spontaneous ADR reporting from all the departments of this tertiary care hospital for monitoring and assessment of ADRs. This study also warrants further research in this part of India for the development of possible intervention strategies to reduce burden of ADRs. Present study revealed that, more awareness about the importance of Pharmacovigilance have to be provided among the health care professionals by way of ADR bulletins, seminars and workshops. Also, more studies with comprehensive sample size need to be conducted in Indian population to know the exact incidence and prevalence of ADRs.

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