

RESEARCH ARTICLE

A retrospective observational study of clinicopathological spectrum of ovarian tumors

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ABSTRACT

Objectives: We aim to study the clinical features and histopathological pattern of ovarian tumors in different age groups which shall add on to the current data on demography and clinical spectrum of ovarian tumors. **Methods:** The retrospective study was done over a period of 5 years (2012-2017); where we included women who underwent surgery for ovariectomy alone or along with hysterectomy. Histopathological examination of the specimens and reporting was done based on WHO classification of ovarian tumors. The data was entered in MS EXCEL spreadsheet and analysed. **Results:** Out of 172 ovarian tumors, 82.6% were benign, 12.8% were malignant. Common clinical presentation in majority of patients (48.84%) was pain in abdomen. Epithelial tumors formed the main bulk of neoplasms (61.6%). The majority of epithelial tumors were serous tumors (54.7%) followed by mucinous (41.5%). Benign tumors were more (53.52%) in the reproductive age group (21-40 years) and malignant tumors were more common in postmenopausal age group. Mature cystic teratoma was the most common type of benign tumor followed by serous cystadenoma. Serous cystadenocarcinoma was the most common type of malignant neoplasm followed by granulosa cell tumour. **Conclusion:** There is a different clinical presentation and age distribution of various histopathological types of ovarian cancers; with benign exhibiting reproductive age group and malignant exhibiting perimenopausal age group. Yet, to confirm, all the ovarian masses must be examined histopathologically for definite diagnosis and management.

Keywords: Ovarian tumors, clinical spectrum, histopathological, reproductive age.

Ovarian masses are commonly found neoplasms in women; these constitute some of the most challenging cases in gynecology. Most of the ovarian tumors presenting during the reproductive age group are benign; whereas, approximately 30% in the post-menopausal age group are found to be malignant.¹ Ovarian cancer is common cancer in women of India and presents at an advanced stage.² Asian countries have ovarian cancer rates of 2–6.5 new cases per 100,000 women per year.³ It represents the sixth most common female cancer and the fourth leading cause of death

in women.⁴

Ovarian tumors present in a wide spectrum of histopathological patterns. In the early stages, several ovarian tumors are asymptomatic and diagnosed in the advanced state.⁵ About 90% of the adnexal masses are detected by pelvic ultrasound (USG).⁶ However, the definitive diagnosis of the tumor is by histopathological study.⁷ It is essential to determine different histological patterns of ovarian tumors, which helps in the planning of diagnosis, prognosis and treatment of ovarian tumors.

Received: 15th May 2020, Peer review completed: 15th June 2020, Accepted: 27th June 2020 .

Upreti P, Reddy GT. A retrospective observational study of clinicopathological spectrum of ovarian tumors. The New Indian Journal of OBGYN. 2021; 7(2): 157-62.

Degree of differentiation of the tumors also helps in the prediction of prognosis of the tumors. The stage and laterality of the tumor also indicate their nature.⁸ The present study was conducted with the aim of studying the clinical features and histopathological pattern of ovarian tumors in different age groups which shall add on to the current data on demography and clinical spectrum of ovarian tumors.

Materials and methods

This study was done retrospectively in the department of Obstetrics and Gynecology. All the cases of ovarian tumors (on either or both sides) which were admitted in the department during the period of 5 years (2012-2017) were included in the study after an informed consent from the patients. Inclusion criteria comprised of the women who underwent surgery for ovariectomy alone or along with hysterectomy. Conservatively managed cases were excluded from the study. Data related to age; clinical symptoms; and histopathology were collected. Histopathological examination of the specimens was carried out at by the Department of Pathology of the hospital by following appropriate staining (Hematoxylin and eosin staining). The histopathological reports (HPR) were based on WHO classification of ovarian tumors (2010).

Statistical analysis: Categorical variables were presented in number and percentage (%) and continuous variables as mean ± SD and median. The data were entered in MS EXCEL spreadsheet and tables were generated.

Results

A total of 172 cases of ovarian tumors were included in the study. The most common clinical presentation was pain abdomen (figure 1).

We found that benign tumors (82.6%) were the most common; followed by malignant tumors (12.8%) and borderline tumors (4.6%). According to

Table 1: Histological categories of ovarian tumors

Histological types of tumours	Benign		Borderline		Malignant		Total	
	No	%	No	%	No	%	No	%
Surface epithelial tumours	86	60.6	8	4.6	12	54.5	106	61.6
Germ cell tumours	52	36.6	0	0	4	18.2	56	32.6
Sex cord stromal tumours	4	2.8	0	0	6	27.3	10	5.8
Total	142	82.6	8	4.6	22	12.8	172	100

histology, Surface epithelial tumour was the commonest type of tumour (60.6%) followed by germ cell tumour (36.6%) (table 1). Out of 106 epithelial tumours, 86 (81.1%) were benign, 8(7.5%) were borderline and 12(11.3%) were malignant. Among surface epithelial tumours, serous tumours were more common (54.7%) than mucinous

tumours (41.5%). Serous cystadenoma (47.1%) was the most common benign epithelial tumour followed by mucinous cystadenoma(32%). Among malignant tumours, serous cyst adenocarcinoma was the most common malignant epithelial tumour (7.5%) (table 2).

Among the germ cell tumors, mature teratoma was the commonest histopathological type as shown in table 3.

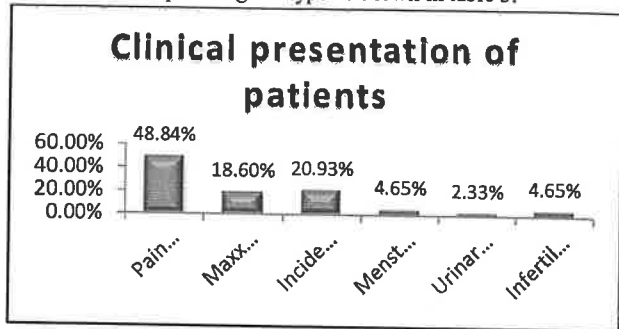


Figure 1: Clinical presentation

Table 2: Distribution of histopathological types of surface epithelial tumours

Types of epithelial tumour	Benign		Borderline		Malignant		Total	
	No	%	No	%	No	%	No	%
Serous	50	47.1	0	0	8	7.5	58	54.7
Mucinous	34	32	8	7.5	2	1.9	44	41.5
Endometroid tumour	0	0	0	0	2	1.9	2	1.9
Brenner tumour	2	1.9	0	0	0	0	2	1.9
Total	86	81.1	8	7.5	12	11.3	106	100

Table 3: Distribution of histopathological types of germ cell tumours

Benign	No	%	Malignant		Total No	%	
			No	%			
Mature Teratoma	52	92.8	Immature teratoma	2	3.6	54	96.4
			Dysgerminoma	2	3.6	2	3.6
Total	52	92.8		4	7.2	56	100

Table 4: Distribution of histopathological types of sex cord tumours

Benign	No	%	Malignant		Total No.	%	
			No	%			
Sex cord tumor with annular tubules	2	20	Granulosa cell tumor	6	60	8	80
Fibroma	2	20			2	20	
Total	4	40		6	60	10	100

Among the sex cord stromal tumors, Granulosa cell tumor was the commonest histopathological type as shown in

table 4. Age of the patients ranged from 11 years to 71 years, median age being 50 years

Both benign and malignant ovarian tumours were found in all age groups. Overall, ovarian

tumour was most prevalent in the age group of 21- 40 years Incidence of malignant ovarian

was most frequent in 51-60 years age group. The age distribution of ovarian tumors has been shown in table 5.

Discussion

Ovarian neoplasm is considered to be the most fascinating tumor of women with respect to clinical

behavior, malignant potentiality, and histogenesis. Mostly, ovarian neoplasms cannot be detected early in their development. Thus, these account for a disproportionate number of fatal cancers and are responsible for about 50% of deaths from carcinoma of female genital tract.⁹ The histomorphological classification of ovarian tumors forms an important part in the evaluation of the neoplasms.¹⁰

Table 5: Ovarian tumors and age distribution

Age groups (years)	Benign (n=142)		Borderline (n=8)		Malignant (n=22)		Total (n=172)	
	No	%	No	%	No	%	No	%
11-20	8	5.6	0	0	4	18.2	12	7.1
21-30	40	28.2	2	25	2	9.1	44	25.6
31-40	36	25.4	2	25	2	9.1	40	23.2
41-50	34	23.9	0	0	4	18.2	38	22
51-60	14	9.9	4	50	8	36.3	26	15.1
61-70	8	5.6	0	0	2	9.1	10	5.8
71-80	2	1.4	0	0	0	0	2	1.2
Total	142	100	8	100	22	100	172	100

The ovarian tumor is diagnosed as benign, borderline or malignant depending on the presence of predominant cell type, pattern of growth, amount of fibrous stroma and cellular atypia with invasiveness. In the index study, out of 172 ovarian tumors, 82.6% were benign (n = 142), 12.8% (n = 22) were malignant, and 4.6% (n = 8) were borderline malignant tumors. In the study by Wills V et al. out of 140 ovarian lesions, 96.4% were benign, 2.8% malignant, and 0.7% were borderline malignant tumor.¹¹ Sheikh S et al. reported that out of the 193 cases, 80.3% were benign, 15.5% cases were malignant, and 4.1% were borderline.¹² In a similar study by Yogambal M et al. total numbers of ovarian tumors studied were 402; out of which 78.6% were benign; 20.65% were malignant and 0.75% were borderline.⁸ Gupta N et al. found that benign tumors constituted 71.9% in each prospective as well as retrospective study, borderline tumors constituted 4.4% and 4.1%, and malignant tumors constituted 23.7% and 22.9% of tumors respectively.¹³

The clinical presentation of the ovarian tumors remains variable. Some of the ovarian tumors can be incidentally diagnosed on USG, while others may present with acute abdominal pain. Common clinical presentation in majority of patients (48.84%) in this study was pain in abdomen. A good number of ovarian masses were diagnosed incidentally (20.93%) during histopathological examination of hysterectomy and salpingo-oophorectomy specimens. Mass abdomen was noted in 18.60% patients followed by menstrual abnormalities (in 4.65%), infertility (4.65%), and urinary symptoms (2.33%). Findings similar to our study were reported by Yogambal M et al. where the commonest presenting symptom was pain abdomen 66.92% followed by mass abdomen 28.11%.⁸ Wills V et al. reported that

menstrual complaints was the most common clinical presentation of patients (in 27.55% patients). Twenty-six percent of ovarian masses were diagnosed incidentally.¹¹ Menstrual complaints followed by abdominal pain were noted by Kanthikar SN et al. in their studies. The exact nature of all ovarian tumor cannot be confirmed preoperatively just by clinical examination.¹⁴

In present study, the tumors were studied in the age group from 11 to 71 years (median age 50 years); where maximum number of cases (25.6%) was seen in child bearing age group of 21-30 years, followed by 23.2% in 31-40 years. Benign tumors were more in the reproductive age group of 21-30 years (28.2%) followed by 25.4% in 31-40 years. The malignant neoplasms, (36.3%), in present study, were seen more commonly in the age group of 51-60 years. Borderline tumors were present in majority (50%) in 51-60 years age group.

Our findings are in accordance with the study of Sheikh S et al. where maximum number of cases (43.5%) was seen in the child bearing age group of 21-30 years, and 30-40 years, 22.3%. Benign tumors were also predominantly present in 21-30 years age group.¹² The malignant neoplasms (46.6%) were present commonly in the age group of 40-60 years. Majority (50.0%) of the borderline tumors were present in 21-30 years.

Wills V et al. found that maximum number of benign ovarian tumors was in the 21-40 year age group and a similar number in the 41-60 year age group. All the malignant tumors (100%) were in the 41-60 year age group. The single borderline tumor was present in the younger group (21-40 years).¹¹ Sharadha SO et al. also noted maximum number of neoplasms (89.9%) in the reproductive age group which was comparable to that reported by Ashraf A et al.^{15, 16}

In present study, 27.3% of malignant ovarian neoplasms were found in younger age group (<30 years). Murthy NS et al also found a fair percentage (26.7%) of malignant neoplasms especially surface epithelial adenocarcinomas in younger age groups.¹⁷ This can be attributed to the possible effects of environmental and life style changes adopted by younger population

For diagnosis, microscopic appearance of the tumor is a must for finding the histopathological pattern on which further management is decided. The grading of tumor type also has its importance in further management.¹⁸ Ovarian tumors show histological heterogeneity. The WHO classification of ovarian tumors is based on the tissue of origin— (1) epithelial, (2) germ cell tumors, and (3) sex cord

stromal tumors. It is globally seen that, surface epithelial tumors are the most common ones.¹⁹ Of the three main groups, epithelial tumors are the most common with serous and mucinous cystadenomas being the commonest epithelial tumors. The single most common ovarian tumor is a germ cell tumor, the benign cystic teratoma, and all other types of germ cell tumors, including malignant germ cell tumors, are rare. Sex cord–stromal tumors are less frequently observed group of ovarian tumors. Of these tumors fibromas, thecomas and granulosa cell are significant. Other sex cord–stromal tumors are rare.¹⁰

This study also is in favor of that observation. Epithelial tumors formed 61.6% (n = 106) the main bulk of neoplasms observed in the study followed by germ cell tumors (32.6%) and sex cord stromal tumors in 5.8% (n = 10). Most of the surface epithelial tumors (60.6%) and germ cell tumors (36.6%) were benign, and majority of sex cord stromal tumors were malignant. Similar results were reported by Sheikh S et al. who noted that the surface epithelial tumors were most common accounting for 54.8% cases followed by germ cell tumors 31.1% cases, sex cord stromal tumors in 3.1%, and metastasis in 2 cases. Majority of surface epithelial tumors and germ cell tumors were benign, and most of sex cord stromal tumors were borderline.¹²

The majority of epithelial tumors were serous tumors (54.7%) followed by mucinous (41.5%) and endometrioid tumor and Brenner tumor (2 cases each). Majority of the serous tumors (47.1%) and mucinous (32%) were benign. All endometrioid tumors and Brenner tumors were malignant.

In study by Wills V et al. most of epithelial tumors were serous tumors (46.4%) and mucinous and germ cell tumors (23.2% each). Most of the serous tumors were benign; only mucinous tumor was borderline tumor. Among the germ cell tumors, all were benign cystic teratomas.¹¹ Sheikh S et al. and Bukhari U et al. also reported similar results with majority being serous tumors followed by mucinous tumors. Most of serous and mucinous tumors were benign.^{12, 20}

Among germ cell tumors, majority were teratoma (96.4%) and 2 cases of dysgerminoma were present. All mature teratoma were benign and 2 cases each of immature teratoma and dysgerminoma were malignant. Wills V et al. reported that among the germ cell tumors, all were benign cystic teratomas with one having a predominance of thyroid tissue (struma ovary).¹¹ Mature cystic teratoma (30.6%, benign) and 1 case of dysgerminoma (0.5%, malignant) were the only Germ cell tumors observed in series by Sheikh S et al.¹²

Among 10 sex cord tumors, 6 were granulosa cell tumor and 2 each were sex cord tumor with annular tubules and fibroma. All sex cord tumor with annular tubules and fibroma were benign and granulosa cell tumors were malignant. Wills V et al. reported only 3 cases of sex cord tumors, among which 2 were fibroma and 1 was granulosa cell tumor.¹¹ In study by Sheikh S et al. 6 cases of sex cord tumors were noted; out of which fibroma and fibrothecoma were present in 1 case each (benign) and granulosa cell tumor and Sertoli cell tumor were present in 2 cases each (malignant).¹²

The present study found that mature cystic teratoma was the most common type of benign tumor (30.2%) followed by serous cystadenoma (29.1%) and mucinous cystadenoma (19.7%) (table 5) A retrospective study by Ahmad et al. showed benign cystic teratoma to be the commonest benign tumor.²¹ Sheikh et al found mature cystic teratoma was the commonest benign tumor in their study followed by serous cystadenoma.¹² In many Nepalese Studies, mature cystic teratoma was the commonest benign ovarian tumour.^{22, 23} However, a study by Thanikasalam has shown serous cystadenoma to be the commonest neoplasm in Indian population while mature cystic teratoma to be commonest among Malayas and Chinese.²⁴ In a study by Yogambal M et al the most common benign tumor was serous cystadenoma followed by mature cystic teratoma.⁸ Some studies from the subcontinent have shown serous cystadenoma to be the most common benign neoplasm.^{13, 20}

Serous cystadenocarcinoma was the most common type of malignant neoplasm followed by granulosa cell tumor in present study (table 5). In a study by Yogambal M et al. Common malignant ovarian tumors were serous cystadenocarcinoma carcinoma and mucinous cystadenocarcinoma.⁸ Serous cystadenocarcinoma was found as the most common malignant neoplasm in a study by Pachori G et al.²⁵

In this study, benign tumors were more (53.52%) in the reproductive age group (21-40 years) followed by perimenopausal group (41-60 years). Serous cystadenoma and Mucinous cystadenoma were present mostly in the patients of 31-50 years, while most of the benign teratomas were seen in 21-30 years age group. Brenner tumor was present in 2 patients of 61-70 years; fibroma in 2 patients of 21-30 years and 2 cases of sex cord tumor with annular tubules was noted in 2 patients of 11-20 years.

In study by Wills V et al. benign tumors were more in the reproductive age group (21-40 years). A similar number of

benign tumors were also seen in the perimenopausal group (41-60 years). All 4 patients diagnosed with malignant ovarian tumors were in the older group (41-60 years).¹¹ The single borderline tumor was present in the younger group (21-40 years). Sheikh S et al. reported similar findings with most of benign tumors in reproductive age group. Most of the benign neoplasms were seen in third and fourth decade with mean age of 32.75 years. Manivasakam J et al. observed an equal distribution of benign ovarian tumors in the reproductive and perimenopausal age groups.²⁶ Malignant neoplasms were expectedly seen with advancing age, peaking in 5th and 6th decade of life as seen in another study.¹² Murthy S et al. also reported similar findings.¹⁷

Conclusion

Most common clinical presentation of ovarian tumors is pain in the abdomen. Benign ovarian neoplasms are seen in both reproductive and perimenopausal age groups; whereas malignant tumors were seen only in the postmenopausal group. Surface epithelial tumor was the most frequently occurring group of tumors. Among surface epithelial tumors, serous tumors, then mucinous and germ cell tumors were commonly found. The occurrence of malignant epithelial tumors in younger age groups was also noted warranting caution to diagnose and manage ovarian masses in young population. Future larger population-based studies are needed to ascertain the etiological factors and changing age trend in the malignant ovarian tumors.

Conflict of interest: None. **Disclaimer:** Nil.

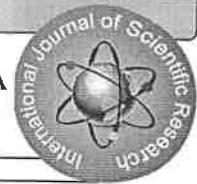
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UNSAFE ABORTIONS AND THEIR COMPLICATIONS: RECENT EXPERIENCES IN A RURAL TERTIARY CARE FACILITY

Obstetrics and Gynaecology / Pathology

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ABSTRACT

Introduction: The number of abortions when classified into facility based, medical abortions outside facilities and other type of abortions constituted a medium of 3375252, 14837497 and 807251 cases respectively, when adjusted for various parameters for India. The present study was conducted to include abortions outside medical facilities including methods of abortion, clinical complaints, complications and their management.

Material and methods: The hospital records for patients who underwent abortions were accessed for a four year period from 2016-2020. The number of patients undergoing supervised abortions and patients presenting with incomplete abortions or related complications were recorded. The presenting complaints for spontaneous abortions and abortions done outside medical health facility along with the therapeutic interventions for such unsafe abortions including complications were assessed.

Results: The total numbers of abortions were 4316, out of which hospital supervised termination of pregnancies constituted 59.8% whereas as abortions or related complications outside a medical facility were 40.2%.

The modes of abortion, presenting features and complications of abortions performed outside medical facilities (total number=1824) and the treatment were recorded. Out of these patients with spontaneous abortions were 36.8% whereas those presenting with complications constituted 63.2%. The commonest method for such abortions was use of abortions pills but other abortifacients and crude instrumentation were also recorded. The commonest clinical feature was discharge per vagina, with retained products of conception causing most complications. The main therapeutic procedure done was dilatation and curettage.

Conclusion: The rural population needs a robust health facility for abortion related care. The sale of abortion pills needs to be tightly regulated. Similarly, crude instrumentation which is a significant cause of morbidity, in unsupervised abortions can be eliminated by awareness and strengthening the health care system making it more approachable for women in rural population.

KEYWORDS

Unsafe abortions, Methods, Complications, Treatment

INTRODUCTION

With recent development in medical sciences, abortion as a cause of maternal mortality is significantly reduced in resource rich developed countries. But in India which has primarily rural population lack of awareness and education along with social taboos and limited health facilities, unsupervised abortions significantly contribute to maternal mortality and morbidity. An unsafe abortion is defined as "a procedure for terminating an unintended pregnancy carried out either by persons lacking the necessary skills or in an environment that does not conform to minimal medical standards, or both."¹ Previous study on unsafe abortion and abortion-related mortality in India, estimated overall rate of abortion to be 4.8%, ranging from 1.6% to 6.5% among the nine states. Overall, 67.1% of abortions were classified to be unsafe, varying widely across the states with the highest being 78.3% and the lowest being 45.1%.² Another aspect of such unsafe abortion outside of health facilities was highlighted by method of abortion as increased use of medications 73% and 5% abortions were done using other methods.³ Unsafe abortions employ various methods include drinking toxic fluids, inflicting direct injury to the vagina or elsewhere—for example, inserting herbal preparations into the vagina or cervix; placing a foreign body such as a twig, coat hanger, or chicken bone into the uterus; or placing of inappropriate medication. Unskilled providers also improperly perform dilatation and curettage in unhygienic settings, causing uterine perforations and infections; external injury methods such as jumping from the top of stairs or blunt trauma to the abdomen are also used.^{1,4}

With these considerations, we studied the profile of abortions in our institute which was the first Medical College in the Shahjahanpur district, Uttar Pradesh India having population of 3.01 million with urban / metropolitan population of only 329,736 and average literacy rate of 67.25%.⁵

MATERIAL AND METHOD

The hospital records for patients who underwent abortions were accessed for a four year period from 2016-2020. The number of

patients undergoing supervised abortions (Medical Termination of pregnancy) and patients who underwent unsafe abortions presenting with incomplete abortions or related complications were recorded.

Further the presenting complaints for spontaneous abortions and abortions done by untrained people outside medical health facility were recorded. The reasons for such unsafe abortions and also the means/modes were recorded, by a detailed history. The products of conception were subjected to histopathological examination for confirmation and to rule out any other associated pathology.

Therapeutic interventions for such outside medical facility abortions were recorded for addressing complications and definitive care of the patient.

OBSERVATIONS

The total number of abortions were 4416, out of which hospital supervised termination of pregnancies constituted 58.7% (2592 cases). Out of these, 1536 (59.2%) were medical abortions using *Mifepristone* and misoprostol under supervision while surgical termination of pregnancy using dilatation and curettage was done in 1056 cases (40.8%). All such cases underwent ultrasonographical examination, before abortion either by medicines or by dilatation and curettage. The only complication in such cases was failure of abortion or incomplete abortion in *Mifepristone* and misoprostol induced cases (3.4%/54 cases) and subsequently these patients underwent dilatation and curettage.

The total number of unsafe abortions or as patient presenting with spontaneous abortions, incomplete abortions or related complications outside a medical facility were 1824 (41.3%).

Out of these, patients presenting with spontaneous abortions were 672 (36.8%) whereas cases presenting with clinical features of incomplete abortions due to interventions outside health facilities were 1152 (63.2%).

The commonest method for such abortions was use of contraceptive and abortion pills (760cases,66%) but use of other abortifacients (physical, chemical and herbal) and invasive methods using crude instrumentation(144 cases,12.5%) for dilatation and curettage with or without abortifacients were also recorded. (Table 1).

Table 1

Serial number	METHODS FOR UNSAFE ABORTION	NUMBER OF CASES(1152)/ PERCENTAGE (100%)
1	Abortifacient Medications	66% (760)
2	Unsafe dilatation and curettage	12.5% (144)
3	Ayurvedic tinctures with insertion of twigs into cervix	8.5% (98)
4	Herbal mixtures from local plants	2.5% (29)
5	Insertion of metallic objects	4% (46)
6	Insertion of foreign bodies like neem twigs/broom sticks	3% (35)
7	Insertion of herbal medication into cervix/vagina	2% (23)
8	Ingestion of toxic liquids like turpentine oil, bleach solun	1.5% (17)

The commonest clinical feature was discharge per vagina but two other findings which were associated with significantly greater morbidity were incomplete evacuation with retained products of conception and injury to cervix in 87 and 20 cases, respectively. (Table 2)

Table 2

S. No.	Symptoms	Percentage% (Number) 100% / 1824	Signs	Percentage % (Number) 100% / 1824
1	Heavy Bleeding Per Vaginum	58.54% (1068)	Blooding per Vaginum	55% (1003)
2	Severe abdominal pain and cramps	16.18% (295)	Abdominal tenderness	15-07% (275)
3	Weakness	12.36% (225)	Pallor	14.02% (256)
4	Fever / Chills	8.19% (149)	Foul smelling Discharge Per Vaginum	8.82% (151)
5	Incomplete evacuation as per Ultrasonography	4.73% (87)	Fever	5-97% (20)
6.			Injury to Cervix	1.12% (20)

Retained Products of Conception were the most common complication 73.68% with spontaneous incomplete abortions as well as unsafe incomplete abortions followed by sepsis 15.13%. The tissue removed was histopathologically confirmed and additional findings like necrosis or inflammation were recorded. Patients presenting or developing shock during the course of treatment were 165 and out of these 18 patients died during the course of treatment. (Table3)

Table 3

S.no.	Complications	Percentage/ (Number) 100% (1824)
1	Retained Products of Conception	73.68% (1344)
2	Sepsis	15.13% (276)
3	Shock	9.03% (165)
4	Genital tract injuries. (1) Cervical lacerations (2) Uterine Perforations	1.18% (21) 0.49% (09)
5	Undiagnosed ectopic pregnancy	0.49% (09)

Dilatation and curettage was the main stay of management along with medicines, blood transfusion and supportive treatment. However cases of uterine perforations and ectopic pregnancy were managed by laprotomy. Hysterectomy was performed in three cases of uterine perforations which were multiple and patient had completed family. (Table 4)

Table 4

S.no.	Treatment / Management	Percentage/ (Number) 100% 1824)
1	Dilatation and curettage and medicines	78.75% (1436)
2	Dilatation and curettage and Blood Transfusion	16-11% (194)
3	Dilatation and curettage with Repair of cervical lacerations	4.16% (76)
4	Laprotomy for Uterine Perforation	0.35% (06)
5	Laprotomy for ectopic pregnancy	0.49% (09)
6	Hysterectomy for Uterine Perforation	0.14% (03)

DISCUSSION

In this study we first tried to estimate the problem of abortion in a district where the majority of population was rural with limited access to maternal health care facilities. We found that medically supervised abortions in authorized health care facility was 58.7%, which was higher than 40% as reported by World Health Organisation(6) and 22.5% as reported by Singh etal (3). The reason for this can be attributed to greater social networking by public relation officers employed by our private institution for awareness of better health care facilities to the rural population and at the same time implementation and benefits of low treatment costs, available at our institution under various government schemes.

The combination of mifepristone and misoprostol has been shown very efficacious in terminating early pregnancy(≤49 days since the last menstrual period) 7, and the same was used for terminating early pregnancies in our hospital. The success rate of this combination of drugs has been documented as ranging from 96.8% to 98.3% 8, and the findings were comparable in our study with a success rate of 96.6%.

In our study, patients presenting with spontaneous abortions were 672 (36.8%) out of total abortions, outside medical health care facilities and the main reasons for presenting to the hospital were delay in periods or discharge per vagina. On further evaluation, the cause was found to be retained products of conception or incomplete abortion. The finding was lower than previously reported as ranging from, 43%-50% 9. The reason for this can be attributed to early age of marriage in rural population thereby negating the strongest risk factor for miscarriage, that is advanced maternal age 10, however the possibility of underreporting in our study can also not be overlooked as many women undergoing spontaneous abortion may not have reported to the hospital in absence of any complications due to reasons such as denial, forgetfulness, and/or miscarriage mistaken for delayed menstruation, as previously reported.9

Singh etal. estimated the incidence of unsafe abortion in India, on basis of outside health care facility to be 78% where 73% abortions were done using medicines and 5% using other methods. 3 The Annual Health Survey for Madhya Pradesh, India reported 45% of abortions occurred at health facilities, indicating a potentially large utilization 55% of unsafe abortion services. 11. Our study estimated the incidence of unsafe abortions to be 41.3 %, which was significantly lower than previous studies. The reason for this is higher level of functionality and better outreach in the catered population, ours being a private sector institution and same has been by documented by Chaturvedi etal. 11.

Medical abortion or abortion by orally administered regimens of Mifepristone and Misoprostol has recently been accepted worldwide as an effective and safe option for early abortion. It is a safe procedure, with mortality rates comparable with spontaneous abortion.12 An important finding in study by Singh etal. was that most abortions are medication abortions, and most medication abortions are obtained outside health facilities using the combined medication abortion protocol of mifepristone plus misoprostol but little is known about what kind of information women are getting when they obtain this method from chemists and informal vendors, and whether they are taking it correctly. 3 We also found that majority of abortions outside health facilities and patients presenting with abortion related complications had used the combination of Mifepristone and Misoprostol without supervision and proper dosage (66%). The procurement of these drugs and their method of use could not be documented as women were not forthcoming and gave only vague replies like from unidentifiable female health worker, local chemist shops or from some relatives. An important complication of this unsupervised mode of usage of these drugs was their use in undiagnosed ectopic pregnancy, which in our study were 9 cases and

laprotomy had to be performed, as a life saving measure in all these patients. Debnath J et al found that history of intake of mifepristone and misoprostol was present in 43.75 % of cases of ectopic pregnancy related abortions cases and concluded that ectopic pregnancy may remain under-diagnosed with potentially serious consequences in patients who have taken these drugs without prior confirmation of intrauterine gestation. 13

Unskilled providers also improperly perform dilation and curettage in unhygienic settings, causing uterine perforations and infections 14. Similarly, other methods of abortion used by unskilled health workers like oral, local or intravaginal use of herbal, medical or corrosive substances / liquids as abortifacients has also been documented 1,4. Unsafe abortions using dilatation and curettage apart from being incomplete abortions can lead to serious complications like hemorrhage, septicemia, septic shock, and visceral injuries including uterine perforations which at the time of curettage during first trimester abortion go unrecognized and untreated.[15] We found that sepsis, shock and genital tract injuries constituted 26.94 percent of such unsupervised abortions and surgical management was mainstay of treatment in 4.65% of cases and included repair of lacerations, laprotomy and hysterectomy.

The complications of unsafe abortions include hemorrhage, sepsis, peritonitis, and trauma to the cervix, vagina, uterus, and abdominal organs. 16 Similarly post abortion care is also not offered to women as untrained village level health care providers who perform these unsafe observations exacerbate the post abortion complications and in the process increase not only the cost but also associated morbidity 17 Bleeding per Vaginum along with pallor constituted the most common clinical features in our study constituting nearly 70% of all women undergoing unsafe abortions. These are difficult for a rural woman to explain or discuss due to social customs and they reported to the hospital only as a last resort. Acute presentation of other complications like fever, tender abdomen, sepsis and shock were also a significant contributor to morbidity and again the patients reported to the hospital as last life saving measure.

CONCLUSION

The present study shows that the rural population needs a robust health facility for abortion related care and at same time better management of complications. The institutional facilities whether public or private with proper motivation can help reduce this morbidity and can encourage rural women for approaching health care facility for abortion and related care. The sale of abortion pills (although government regulations exist but implementation needs to be strengthened) needs to be tightly regulated and again crude instrumentation which is a significant cause of morbidity, in such unsupervised abortions can be eliminated by education, awareness and strengthening the health care system making it more approachable for women in rural population.

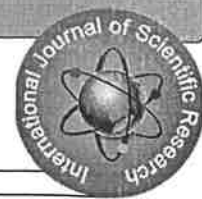
LIMITATIONS

The present study included only those patients who reported to this hospital, which was the first tertiary care center in the district but it cannot be extrapolated to reflect on the entire district population, where the burden may be higher.

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EVALUATION OF VITAMIN-D & CALCIUM LEVEL IN WOMEN WITH POLYCYSTIC OVARIAN DISEASE IN A TERTIARY CARE CENTRE

Bio Chemistry

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ABSTRACT

Introduction: PCOD is the most common endocrine disorder in females of reproductive age group. PCOD leads to metabolic & hormonal disturbance. **Objective:** To assess level of vitamin D & Calcium in PCOD cases as compared to age matched controls **Material & Method:** Total of 60 PCOD cases were enrolled along with 60 control subjects, cases were selected according to revised Rotterdam criteria. Vitamin D was evaluated with CLIA technique, Calcium estimation was done by system pack kit method. All values were expressed as Mean + SD. p value <0.05 was considered significant. **Conclusion:** Low levels of vitamin D & Calcium was observed in PCOD cases when compared with healthy controls.

KEYWORDS

Vitamin D, PCOD, Calcium

INTRODUCTION

Polycystic ovarian disease (PCOD) is a common endocrine disorder seen in women of reproductive age group. PCOD can lead to Diabetes mellitus, endocrine gland cancer and cardiovascular diseases it is associated with anovulation, increased insulin secretion, and central obesity(1). The patients symptoms begins with menstrual irregularity, laboratory investigations shows elevated androgen levels, and clinically presents with hirsutism and acne, these clinical outcomes were proved by the presence of polycysts in the ovaries by ultrasonography(2). Other clinical signs of this syndrome include many metabolic disorders such as hypertension, dyslipidemia, metabolic syndrome, glucose tolerance and insulin resistance, and consequently hyperinsulinemia. The human body gets vitamin D from endogenous or exogenous sources. Exogenously from diet, while endogenously from photochemical conversion of cholesterol to 7-dehydrocholesterol in the skin by sunlight followed by hepatic or renal hydroxylation. In the skin, Photolysis of dehydrocholesterol resulted in the formation of vitamin D₃ by UV light. The vitamin D₃ molecules then undergoes hydroxylation, the first in the liver to 25OHD through D₃-hydroxylase and the second in the kidney to 1,25-dihydroxy vitamin D₃ which goes in the circulation by binding to vitamin D binding protein (3)(4). The cause for PCOD is unknown, however literature suggest the involvement of genes and environment (lifestyle) as strong causative factors(5). There are suggestions that calcium has important role in activation and maturation of oocyte in animals (6) therefore, abnormalities in calcium metabolism may play an important role in patho- genesis of PCOD. Many studies have suggested that both calcium and vitamin D supplements may improve insulin sensitivity in women with PCOD(7). Vitamin D is seen to be important for regulation of pathways involved in glucose metabolism and therefore, insulin secretion. Thus, its deficiency could lead to glucose intolerance, insulin resistance & metabolic syndrome also (8)(9). The cellular effect of vitamin D is mediated through the intra-nuclear vitamin D receptor (VDR). The presence of VDR in the ovary, uterus, placenta and testis suggests role of vitamin D in reproductive physiology vitamin D deficiency is believed to contribute for a spectrum of gynecological disorders of which PCOD appears the best studied(10)(11)(12). This case control study is done to investigate levels of Vitamin D & Calcium status between PCOD & non PCOD subjects.

MATERIAL & METHOD

This case control study was carried out in collaboration between Biochemistry and Obstetrics & Gynaecology department of Varun Arjun Medical College & Rohilkhand Hospital, Banthra, Shahjahanpur(U.P) from a period of October 2021 to November 2022. A total of 60 women with PCOD were selected from Gynaecology OPD, these were taken as cases. Similar age matched healthy fertile

women were selected as controls. Diagnosis of PCOD was made according to the revised Rotterdam criteria 2003 (13). Those with at least two of the following criteria were defined as PCOD patients:

- (i) Oligo-anovulation
- (ii) Hyperandrogenism
- (iii) Polycystic ovaries(>12 follicles measuring 2-9mm in diameter)

Inclusion criteria

All women in reproductive age group (18-44 years) satisfying Rotterdam criteria were included.

Exclusion criteria

- Subjects having diabetes mellitus, renal/liver disease or other endocrine disorders
- H/o drug intake i.e. vitamin D or calcium supplements, contraceptive pills etc
- Pregnancy

5mL blood sample was taken in a plain vial from both cases & controls, sample collected was allowed to clot for 20 minutes and then centrifuged at 4000 rpm for 10 minutes, and then serum was separated. Estimation of Serum Calcium was done by System pack Arsenazo kit method in ERBA EM200 fully autoanalyser machine. Vitamin D estimation was done by Chemiluminescence immunoassay (CLIA) in Maglumi X3 fully automated machine by Snibe diagnostics in Clinical Biochemistry department of Varun Arjun Medical College. SPSS version 20.0 is used for statistical analysis & all values were shown as mean and standard deviation.

RESULT

Data was collected from 60 PCOD cases and 60 control healthy female group. Mean age was 25.6 ± 5.8 in PCOD group and 25.1 ± 6.1 in control group. Table 1 shows distribution of cases according to age group with maximum number of cases seen in 24-28 age group (i.e. 46.6%). Levels of vitamin D was considered as <10ng/mL as deficient, 10-30 ng/mL as insufficient and > 30ng/mL as sufficient. Out of 60 cases a total of 30 (50%)PCOD cases were observed as vitamin D deficient, 27 (45%) were seen to be having insufficient vitamin D and only 3 (5%) were in the range of sufficiency. Whereas in control group 19 (31.6%) were deficient, insufficiency was seen in 29 (48.3%) women and 12 (20%) were in the range of sufficiency.

Table 1: Age wise distribution of cases

Age	No. of cases	Percentage
18-23	12	20%
24-28	28	46.6%
29-33	13	21.6%
34-40	7	11.6%

Table 2: Distribution of cases & control according to Vitamin D levels

Vitamin D(ng/mL)	PCOD cases(n=60)	Control group(n=60)
Deficient (<10 ng/mL)	30	19
Insufficient(10-30 ng/mL)	27	29
Sufficient (> 30 ng/mL)	3	12

Table 2 shows mean values of Vitamin D and Calcium in Polycystic ovarian disease patients and control group. The mean value of Vitamin D is 18.2 ± 6.2 in PCOD subjects as compared to 26.3 ± 8.3 in healthy control and this difference was statistically significant. Whereas mean of Calcium was 8.0 ± 0.9 in PCOD cases as compared to 8.5 ± 1.1 in healthy controls and this difference was also seen to be statistically significant. Both the measured parameters were showing statistical significance (p value<0.05) when compared with age matched healthy controls.

Table 3: Comparison between two studied groups(Mean ± SD)

Parameter	PCOD patients(n=60)	Control group(n=60)	p value
Age	25.6 + 5.8	25.1+ 6.1	>0.05
Vitamin D	18.2 + 6.2	26.3 + 8.3	<0.05
Calcium	8.0 + 0.9	8.5 + 1.1	<0.05

DISCUSSION

PCOD is a disorder characterised by chronic anovulation, hyperandrogenism and multiple small cystic follicles in the ovary, mainly affects 4% - 16% women in reproductive age group(14). The biological actions of vitamin D are exerted through a soluble protein—the vitamin D receptor (VDR). VDR can be found in various tissues including both the nuclei and cytoplasm of granulosa cells (GC) of human ovaries which indicates that it is responsible for the physiologic functions of 1,25(OH)2D3 in ovarian follicles(15). Hypovitaminosis D is connected to the onset of chronic diseases and that its deficiency may interfere with the normal physiology of the human body(16), we anticipated the women with PCOD in our study would have lower vitamin D levels compared with the control group. In many PCOD cases, high prevalence of vitamin D deficiency is seen as compared to control group(17). Our study shows significantly low level of vitamin D when compared with control group, which is consistent with many observational studies which showed low vitamin D concentration in women with PCOD(18).

Clinical manifestations of PCOD include obesity, metabolic syndrome and chronic inflammation, which are related to vitamin D deficiency(19-21). In our study we found low serum calcium level in PCOD cases which is also consistent with other studies(22-24). Low plasma level of vitamin D results in hypocalcemia, low calcium levels have been associated with inhibition of folliculogenesis in PCOD cases. This low concentration of vitamin D results in menstrual irregularities and fertility impairment(25,26). Li et al., (27) and Wher et al., (28) also reported lower vitamin D level in PCOD patients contrasted to control healthy women which is comparable to our study result. Mazloomi S et al., (29) reported low levels of vitamin D in women with PCOD, with average vitamin D levels between 11-31 ng/mL, and the majority having values <20 ng/mL (67–85%). This result is also comparable to our study. A study was done on 80 newly diagnosed PCOD women with mean age (23 to 33 years). Many items were assessed in this study which includes the following items FBS, Calcium, phosphorus, vitamin D. Results of PCOD and matched healthy Women were compared. Women with PCOD have low level of vitamin D in comparison to the healthy controls and there obvious difference with age and BMI(30). In agreement with us He CL et al.(31) has confirmed that PCOD is associated with vitamin D deficiency, the study confirm that approximately 67–85% of PCOS women have vitamin D level below 20 ng/mL.

CONCLUSION

Our case control study concludes that both Vitamin D and Calcium is low in PCOD cases when compared with normal control group. Though our study has certain limitation due to small sample size. By taking more sample size we can ascertain the beneficial effect of vitamin D and calcium supplementation in these PCOD cases.

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TO EVALUATE THE EFFECTIVENESS OF SALIVARY UREA & CREATININE LEVELS AS A DIAGNOSTIC MARKER FOR CHRONIC KIDNEY DISEASE

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ABSTRACT:

Background: Chronic kidney disease (CKD) is defined as kidney failure with the organ functions reduced or lost completely and the kidneys are incapable of filtering excess fluids. CKD leads to many metabolic changes in blood that often warrants frequent biochemical analysis. Estimation in blood is an invasive and worrisome procedure. It would be quite easier if a noninvasive alternative to blood analysis is identified. Saliva can be collected noninvasively, repeatedly, and without the help of healthcare personnel.

Objective: This study analyses saliva as a medium to measure urea and creatinine levels in Chronic kidney disease(CKD) patients. The main objective of this study was to compare serum and salivary urea and creatinine levels in CKD patients and healthy controls, and to decide whether salivary creatinine and urea levels can be used to diagnose or monitor CKD in as efficiently as serum creatinine and urea levels.

Material & method: This study included 60 Chronic kidney disease(CKD) patients & 60 age matched healthy controls from Varun Arjun Medical college & Rohilkhand Hospital, Banthra, Shahjahanpur(U.P). Urea estimation in blood was carried out using system pack kit of transasia company using urease GLDH method. Creatinine levels was measured using enzymatic reaction colorimetric method done on ERBA-EM200 Transasia fully autoanalyzer. Unstimulated saliva along with blood sample were collected. Estimation of salivary urea & creatinine was done using the same method as discussed above.

Result: In CKD patients, the mean salivary creatinine level was 1.51 ± 0.45 mg/dL and the mean salivary urea level was 67.33 ± 21.85 mg/dL, versus 0.21 ± 0.1 mg/dL and 16.4 ± 6.7 mg/dL respectively, in the control group. Serum urea and creatinine, and salivary urea & creatinine were significantly higher in the CKD patients than in the controls ($p < .05$). There was a positive correlation seen between serum and salivary creatinine and serum & salivary urea also.

Conclusion: Based on the results of our study, we propose that salivary urea and creatinine has a strong potential to be used as a marker in diagnosis and monitoring of chronic kidney disease patients.

Keywords: Salivary, urea, creatinine

INTRODUCTION:

Chronic kidney disease is defined as increased levels of blood creatinine and serum urea, along with hematological, electrolyte, endocrine and skeletal disorders which leads to accumulation of metabolic waste products and thereby causing multiorgan involvement(1)(2). The use of blood sample in order to determine the levels is still the gold standard method. Saliva due to its availability and non-invasive method of collection, it is gaining wide momentum in current times to be considered as a diagnostic tool for diagnosing chronic kidney disease(3)(4).

Salivary levels can indicate any changes in urea and creatinine levels which are the usually done through blood sample collection in chronic kidney disease patients. Thus saliva may play an important role as a diagnostic tool in diagnosing patients with chronic renal disease. Chronic kidney disease occurs when the function of the kidneys is impaired towards 5--10% of the original capacity, defined by a reduction in glomerular filtration rate and decreased creatinine clearance rate(5). Saliva is a dilute fluid, over 99% being made up of water and the rest are dissolved solids i.e. organic and inorganic constituents(6).

In our country number of CKD patients are increasing rapidly as reflected by rising elderly populations and rising number of patients with hypertension and diabetes. Biochemical markers has a significant role in making proper diagnosis and in assessing risk and modulating treatment to improve clinical outcome. Blood sample collected for biochemical estimation is an invasive procedure and the patient has to repeatedly give sample making it very cumbersome for the patient as compared to saliva which is secreted by salivary gland and is easy to collect and non-invasive also. The main objective of our study is to measure urea and creatinine level both in saliva & serum and to evaluate the effectiveness of saliva as a diagnostic method for diagnosing chronic kidney disease.

MATERIAL & METHOD:

This cross-sectional study was carried out in 60 patients of chronic kidney disease who were undergoing treatment in the hemodialysis unit of Varun Arjun Medical College & Rohilkhand Hospital. Sample collection of saliva & blood was carried out by Biochemistry department of our hospital. Total of 60 chronic kidney disease patients

aged > 18 years were selected over a period from March 2022 to November 2022 who were undergoing hemodialysis at our institution, similar age matched healthy controls were also selected.

Inclusion criteria:

- (i) Chronic kidney disease patients undergoing hemodialysis
- (ii) Age > 18 years

Exclusion criteria:

- (i) Any systemic disease(Diabetes mellitus, any endocrine disorder)
- (ii) Taking any drug which could affect saliva quality
- (iii) Alcoholics & smokers

Sample collection:

On the basis of inclusion & exclusion criteria patients were selected who were undergoing hemodialysis. 3mL of blood sample was collected and immediately transferred to plain vial and was allowed to clot for 20 minutes and later centrifuged at 5000 rpm for 10 minutes. Serum sample obtained was used for estimating urea & creatinine levels. For salivary sample early morning unstimulated saliva was collected in a sterile tube by spitting method. Both the samples collected were immediately sent to biochemistry laboratory and was analyzed on the same day.

For urea & creatinine estimation both in saliva and serum, system pack kits were used provided by Transasia all tests were done on EM200 fully autoanalyser. Serum urea was estimated by Urease glutamate dehydrogenase(GLDH) method while creatinine estimation was done by enzymatic kit method. All test values were validated by controls provided by the manufacturer as well.

Statistical analysis:

All test values were expressed as Mean \pm SD. Student's t-test was used for statistical analysis and p value <0.05 were considered significant. Correlation between salivary & serum creatinine as well as urea was done by pearson's correlation test.

RESULT:

The study population consists a total of 120 individuals among which 60 patients were suffering from CKD and 60 were healthy controls. One group consists of 60 CKD patients. There were 34 males and 26 females. The mean age of this group (CKD) was 34.3 years with a standard deviation of 10.1. The other group comprised 60 healthy volunteers as controls. There were 29 males and 31 females. The mean age of the controls was 32.4 years with a standard deviation of 12.2(Table I). In CKD patients the serum urea level shows mean of 155.57 mg/dL (SD 55.26) and salivary urea level with a mean of 67.33mg/dL (SD 21.85). Both serum urea and salivary urea shows positive correlation($r = 0.79$).(Table II). In CKD patients the serum creatinine level shows mean of 11.76 mg/dL (SD 3.63) and salivary creatinine level with a mean of 1.51 mg/dL (SD 0.45).(Table III).

The mean salivary and serum creatinine & urea concentration were found to be significantly higher in CKD patients compared to controls & is statistically significant. If we want to consider salivary urea and creatinine as a reliable substitute to serum urea & creatinine respectively, then a strong correlation needs to be established between these two parameters.

To assess any correlation between salivary and serum creatinine and urea values we performed pearsons correlation analysis of CKD group correlating values of creatinine in serum & saliva and we found a significant positive correlation , $r = 0.55$. (Figure I,II). On correlating urea level in serum and saliva in CKD patients, we here also found a significant positive correlation, $r = 0.79$. (Figure III,IV). By seeing these findings we can say that as urea & creatinine increase or decrease in blood, there is corresponding increase or decrease in salivary urea & creatinine respectively.

TABLE 1: Age & gender wise distribution of CKD patients & Controls

	Chronic kidney disease	Controls
N(no. of individuals)	60	60
Age	34.3 \pm 10.1	32.4 \pm 12.2
Male	34	29
Female	26	31

TABLE 2: Comparision of Salivary urea & Serum urea levels between CKD patients and Controls.

Test	No.of participants	Chronic kidney disease (Mean \pm SD)	Controls (Mean \pm SD)	p value	r value
Salivary urea	60	67.33 \pm 21.85	16.4 \pm 6.7	<0.001	0.79
Serum urea	60	155.57 \pm 55.26	29.1 \pm 6.4	<0.001	

TABLE 3: Comparison of Serum creatinine & Salivary creatinine levels between CKD patients and Controls.

Test	No. of participants	Chronic kidney disease (Mean \pm SD)	Controls (Mean \pm SD)	p value	r value
Salivary creatinine	60	1.51 \pm 0.45	0.21 \pm 0.1	<0.001	0.55
Serum creatinine	60	11.76 \pm 3.63	0.71 \pm 0.4	<0.001	

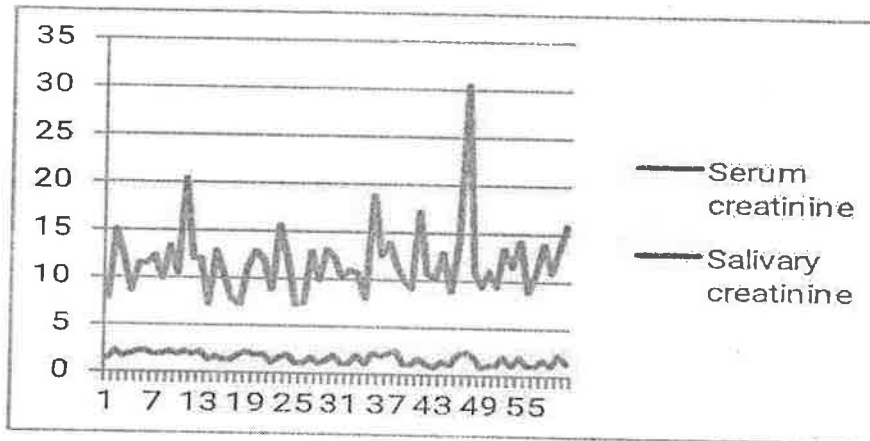


Figure. 1 Correlation between salivary & serum creatinine in CKD patients

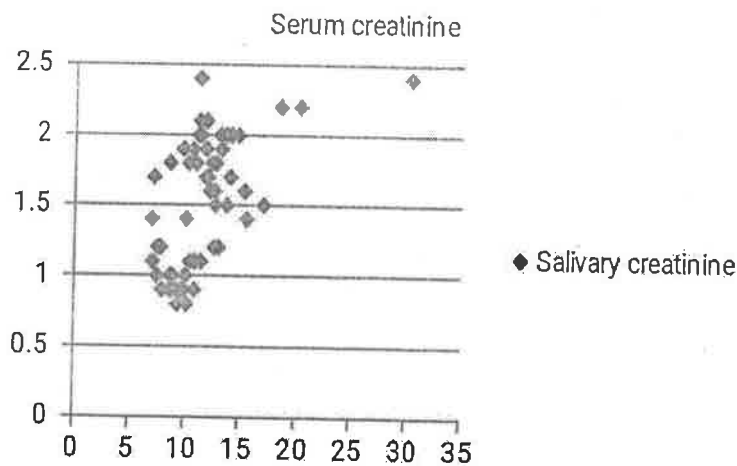


Fig. 2 Scatter plot between serum and salivary creatinine level of CKD patients

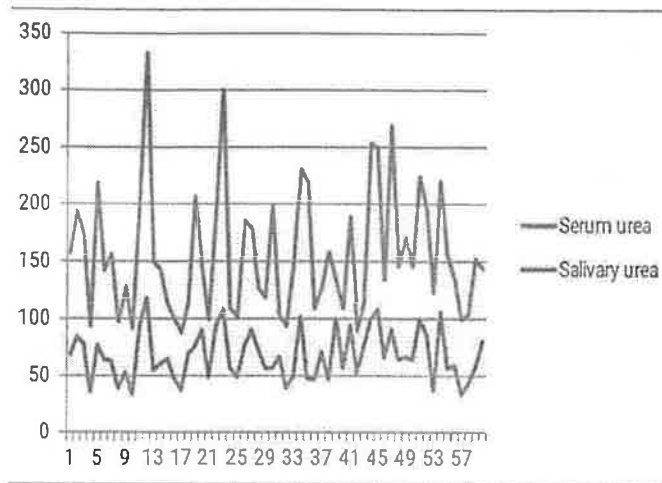


Figure. 3 Correlation between salivary & serum urea in CKD patients

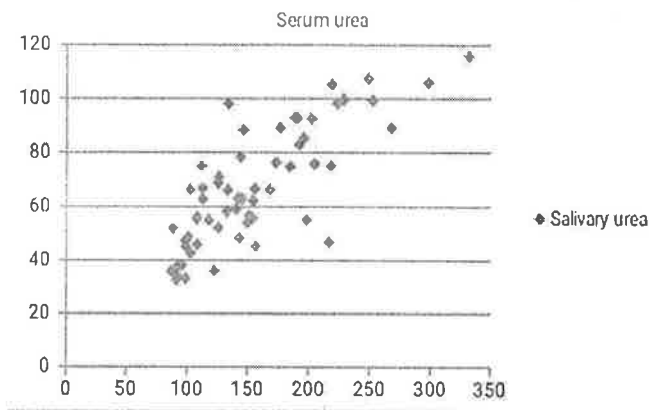


Figure. 4 Scatter plot between salivary & serum urea level of CKD patients

DISCUSSION:

In our study, patients with CKD showed increased levels of salivary urea and creatinine when compared with healthy individuals, also the salivary levels of creatinine and urea showed positive correlation with the levels in blood. Our findings are consistent with previous studies(7)(8) which also supports possibility of using salivary estimation of urea & creatinine as a marker for diagnosis of CKD. Kidneys regulate the volume of the extracellular and intracellular fluid to maintain homeostasis of the body by constant processing of the plasma through filtration, reabsorption and secretion of the substances(9). Whenever there is an increase in the blood urea there is simultaneous increase in salivary urea also because the kidneys are not able to excrete urea in the

renal failure and its concentration in blood increases with increased concentration in saliva because of increased serum urea which creates an increased concentration gradient in turn increasing the diffusion of urea from serum to saliva(10). Creatinine is unable to diffuse easily across the cells of the salivary gland in the healthy state under normal conditions. But in patients of CKD, creatinine value increases in saliva possibly due to an alteration in the permeability of salivary gland cells and the high serum creatinine levels in CKD patients create a concentration gradient that facilitates diffusion of creatinine from serum in to saliva.

Our study showed a significantly high creatinine and urea level both in serum and saliva of CKD patients when compared with controls. Similar observation was made by Davidovich et al(11) and Xia et al(12). The positive correlation between serum and salivary urea & creatinine observed in this study could be explained by the increased concentration of creatinine and urea in patients with CKD which creates a concentration gradient that facilitates increased diffusion of creatinine and urea from serum into saliva(13). Blicharz(14) and colleagues suggested that, measurement of biomarkers in saliva may be an effective & alternative method for monitoring & diagnosing CKD patients. Monitoring of markers in saliva instead of serum is advantageous because saliva collection is noninvasive, simple and inexpensive approach with minimal risk of infection.

Our study supported that there was a significant linear relationship between serum urea and creatinine and salivary urea and creatinine levels respectively. The correlation coefficient for serum urea and salivary urea was ' r ' = 0.79 and for serum creatinine and salivary creatinine was ' r ' = 0.55 which is statistically highly significant ($p < 0.001$). Therefore, salivary creatinine and urea levels correlate well with the serum creatinine and urea respectively so that saliva can be used as a non-invasive diagnostic tool(15). Lloyd JE et al.(3) also conducted a study on 26 renal disease patients and 23 healthy volunteers and found a statistically significant relationship between salivary and serum creatinine concentrations for the patients and salivary creatinine concentrations are 10-15% of those in blood. Similar results were obtained by Cardoso EML et al.(16) concluding that salivary urea estimation is a harmless and useful diagnostic tool. Venkatapathy R et al.(17) and Seethalakshmi C et al.(18) also showed a significant positive correlation for serum urea & salivary urea and also for serum & salivary creatinine. Tomas I et. al (19) in 2008, analysed the alterations of saliva in different stages of chronic renal failure (CRF) and statistically significant ($p < 0.01$) positive correlation was seen between blood and salivary urea concentrations ($r = 0.572$) in chronic renal failure patients and a statistically significant ($p < 0.01$) positive correlation was detected between the serum and salivary creatinine concentrations ($r = 0.40$). Lasisi TJ. et al (20) conducted a similar study in 2016 estimating urea and creatinine levels in blood and in whole unstimulated saliva for patients with end-stage CKD and healthy controls and established a positive correlation between blood and salivary creatinine as well as urea levels in patients undergoing dialysis treatment.

CONCLUSION:

On the basis of our findings, we can say that saliva has a strong potential to be used as an alternative to blood for monitoring and also for diagnosing patients with Chronic kidney disease. Being a noninvasive method of collection saliva can reduce discomfort & risks associated with blood collection method. Our study reveals the most important finding is that saliva can play an important role in measuring serum creatinine and urea levels in individuals with CKD.

Abbreviations:

CKD: Chronic kidney disease, GLDH: glutamate dehydrogenase, SD: standard deviation

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