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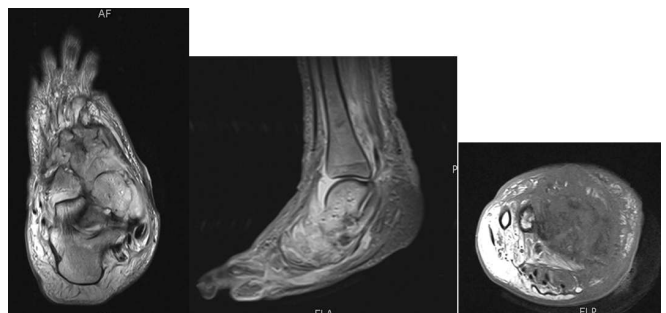
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16 years old boy presented with complains of right foot and ankle swelling and discharge for 2 months. Status post left foot amputation done April 2017 for similar complains. MRI right foot was done that showed features consistent with osteomyelitis. Right sided below the knee amputation was done and PICC line was inserted for prolonged use of IV antibiotics. Patient was diagnosed with Hereditary Sensory Motor Neuropathy on the basis of EMG/ NCV  
Final diagnosis: Hereditary Sensory Motor Neuropathy with right foot osteomyelitis needing below the amputation

Courtesy: Dr. Afia Tariq, Dr Ali Faisal Saleem, Aga Khan University Karachi

## Age Appropriate Childhood Immunization and Catch-up Immunization, Pakistan.

Childhood immunization save more than three million lives each year. In Pakistan, Expanded Program on Immunization (EPI) provides immunity against nine deadly diseases for infants and young children. An estimate of 19.4 million infants worldwide are still missing basic vaccines. One and a half million deaths could be avoided with improved global vaccination coverage. According to Pakistan Demographic and Health Surveillance (2012-13)<sup>1</sup> report, only 43% of children received all vaccination by 12 months of age, however this reduced to 35% for Sindh.<sup>2</sup> Sindh has 2,786 registered births who are under 5 years of age.<sup>3</sup> Unfortunately, Pakistan has yet to know about the current figures or percentages of children who had missed their age appropriate vaccination.<sup>4</sup> It is concerning not to know about alternative schedule that can be used to guide parents on catch-up immunization for missed children. Pakistan lacks an alternative schedule or catch-up immunization schedule for children under 2 years of age. To strengthen the efforts of health care team and betterment of community a catch-up immunization policy is also needed.<sup>5</sup> Some important proximal determinants of low immunization in Pakistan are low literacy rate, lack of empowerment and involvement of women in decision making, higher fertility rates etc. Being afraid of side-effects of vaccines, vaccination phobia or surrounded by many anti-vaccine families or for many other reasons parents miss age appropriate vaccination of their children, however the same mind set is not prevalent in Pakistan. Lack of resources, information and advocacy are also some factors that had contributed towards under-utilization of vaccines against vaccine preventable diseases. This ultimately poses great risk to community; making vulnerable population more prone towards disastrous diseases.<sup>6</sup>

Under immunization has significantly shown to increase risk of contracting and spreading vaccine preventable diseases. Like Measles breakout in Pakistan; this all reminds Government to focus more on supplementary immunization activities (SIAs). To immunize children at an age when their immune response from the vaccine will be most effective, while still early enough to prevent them from contracting diseases when they are most susceptible.<sup>7</sup>

Deferring certain vaccinations, parents are putting their children at a far greater risk of deadly diseases; such as Measles, Pneumonia, and Pertussis.<sup>8</sup> Parents also prefer to administer one vaccine or combination vaccines at a time, this also creates

an area of research to work on developing combination vaccines.<sup>9</sup> Introduction of new vaccine in immunization schedule is a historical moment for the country; currently introduced in Punjab and will be extended to other parts of Pakistan along with the support of WHO, UNICEF and GAVI.<sup>10</sup>

We need to focus on our efforts to help parents recognize the importance of timely vaccination, catch-up immunization schedule is safe for their children and help them understand that delay vaccination is only adding on their child's risk. Challenges identified to get targeted result are quality and utilization of data, community involvement, availability of vaccines and better access to immunization services. Advertising is also an essential component to increase awareness of new vaccines and seriousness of a disease, to direct parents towards important source of information and to minimize misconception related to vaccine. At national level vaccination campaigns need strong integrated planning. Post vaccination campaign require much work to be done like timely accomplishment of vaccine campaigns, monitoring adverse reactions, and carrying out surveillance during and after campaign implementation.

Continuous review of immunization schedules is necessary to stress upon significant issues of childhood immunization. At National level, there is urgent need to reinforce and strengthen the surveillance of VPDs.

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## Social Stigmatization in Tuberculous Patient: A Hospital Based Survey in Lahore, Pakistan.

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### Abstract

#### Background

Inadequate knowledge regarding Tuberculosis leads to stigmatization due to perceived risk of transmission of disease. It is pertinent to comprehend the origin of Tuberculosis stigma so as to reduce its impact on health as geographic and cultural variation may play an important role. Aim was to assess perception of stigma among patients and discriminations faced by them within the family and society.

#### Methods

A cross sectional study was conducted on 300 Tuberculosis patients of Gulab Devi Chest Hospital, Lahore, Pakistan after IRB clearance. Interviews were conducted after taking consent, using a validated questionnaire adopted from a previously published study. Perceptions of the participants were addressed regarding stigma related to Tuberculosis especially regarding their fears associated with disclosing their disease within and outside their families, experiencing of loneliness, losing of friends and feeling hurt on the reaction of their families, friends and outsiders. Chi square was chosen as the test of significance with a  $p$ -value of  $<0.05$  considered significant.

#### Results

Mean age was  $42.5 \pm 17$  with male predominance (median 42, IQR 13.5), 239 (79.7%) having an income less than 25,000. Participants and spouses were mostly illiterate 154 (51.3%) and 161 (53.6%) respectively, 239 (79%) being self-employed. They 213 (71%) were not afraid to disclose their disease to their families and others, while 175 (58.3%) were not worried of being a burden on their family. On the contrary 158 (52.7%) felt hurt at the reaction of others on disclosing their disease ( $p=0.000$ , CI=12.57 – 35.52). Many had lost friends 216 (72%) and were experiencing loneliness ( $p=0.000$ , CI=29.95 – 52.24). Fear of visiting tuberculosis clinics was observed in 200 (67%). Participants had no fear of being perceived as AIDS patients 235 (78.3%) ( $p=0.000$ , CI=8.58 – 32.26). They had no fear of developing AIDS 243(81%) Tuberculosis 190 (63.3%) due to smoking, drinking or other risky behaviors ( $p=0.03$ , CI= 0.50 – 30.22)

#### Conclusions

This study concludes that substantial stigmatization and discrimination was being faced at community as compared to family level attributed to strong family bonds in countries like Pakistan.

#### Keywords

Tuberculosis, Stigmatization, Pakistan

#### Introduction

An important social determinant of health constitutes stigma which is proclaimed by communities, personal attitudes and institutions.<sup>1</sup> When a certain characteristic of individuals or groups is disvalued it is stated as stigma.<sup>2</sup> The targeted individual develops a sense of being looked down upon by the society which leads to internal feelings of disapproval, self-accusation and shame.<sup>3</sup> These feelings attribute to increased risk taking behavior, concealing of the cause leading to stigma as well as disturbance within personal relationships.<sup>4</sup> Stigmatization is an attitude or belief aimed to attain exclusion while discrimination is the behavior due to these beliefs.<sup>5</sup> Individuals tend to suffer from both as they imply them to be undesirable and disvalued by the community and family.<sup>2</sup>

Difficulties in identifying, characterizing, measuring, and tracking changes in stigmatization over time have made it challenging to justify devoting resource-intensive interventions to the problem.<sup>1</sup> One exception being human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) research.<sup>6</sup> Substantially less studies have been conducted on how stigma impacts the health of individuals at risk for or infected with Tuberculosis (TB).

It is pertinent to comprehend the origin of Tuberculosis stigma so as to reduce its impact on health. Geographic and cultural variation may play an important role, but most authors identify the perceived contagiousness of Tuberculosis as a leading cause of stigmatization.<sup>5</sup> Lack of knowledge regarding routes of transmission may also contribute to stigma.<sup>7</sup> People with relatively good knowledge of transmission, transmissibility and perceived risk can lead to stigmatization and isolation of individuals diagnosed with Tuberculosis.<sup>8</sup>

HIV and Tuberculosis coexist and in areas of high prevalence, stigma against Tuberculosis is on the higher side.<sup>9</sup> Mostly HIV

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positivity is linked to Tuberculosis thus promoting HIV associated Tuberculosis stigma.<sup>10</sup> This stigma can be attributed to many other factors like low social class, poverty, malnourishment and foreign born.<sup>12,13</sup> Many communities hold the individual's activities responsible for their punishment in the form of the disease and believe that they deserved to be infected due their moral and personal behaviors.<sup>8,13</sup>

The stigma is so pronounced that the infected person believes that he/she can have major social and economic setbacks especially in the form of isolation from the society at large. An example being Ghana where Tuberculosis infected individuals are prohibited from selling goods in public markets and attending community events.<sup>14</sup>

Stigma may be held responsible for the development of fears which lead to specified behaviors within the community. Cause of death might not be shared or recorded which can be considered as an important tool for Tuberculosis screening.<sup>15</sup> They tend to conceal their disease from their families, friends and society.<sup>5</sup> They develop fears leading to self-accusation, guilt and withdrawal from families attributing to isolation.<sup>16</sup>

In general, men bear more socioeconomic impact than females, including job loss and reduced income.<sup>17</sup> The disease effects both genders. Males and females are concerned regarding the stigma they may face. Women as they believe it would affect their marriages and they would be isolated by their families and lose their homes.<sup>18</sup> On the contrary literature states that men feel threatened regarding their marriage prospects. Married females with families fear rejection from their husbands on being diagnosed with Tuberculosis.<sup>19</sup> We aim to assess the perception of stigma and discriminations faced by Tuberculosis patients in the society at large and in their relatives among the patients of Tuberculosis at Gulab Devi Chest Hospital, Lahore, Pakistan.

### Materials and Methods

Cross sectional study was conducted in Gulab Devi Chest Hospital, a major tertiary care setup in Lahore, Pakistan. The hospital has six medical and chest units. In this hospital based survey, a total of 300 admitted pulmonary tuberculosis patients giving consent were enrolled and interviewed by the principal investigator. Patients suffering from extra-pulmonary tuberculosis and other ailments were excluded from the study.

A pretested validated questionnaire was used to interview the patients.<sup>20</sup> Interviews were conducted in the local language for better comprehension of the subjects. Study was completed within three months.

### Ethical Considerations

IRB approval and permission from Gulab Devi Chest hospital was sought before the conduction of the study. Consents were taken from the participants and data was collected by the

principal investigator assuring anonymity and confidentiality to ensure that ethical guidelines were followed during the study.

### Data Analysis

SPSS software version 20 was utilized to analyze the data. Mean and median of age of participants was calculated, while frequencies and percentages of occupation, income, fears associated with disclosure of disease to family, friends and relatives, experience of loneliness, losing of friends, fear of developing AIDS or TB being perceived as AIDS, fear of developing TB or AIDS due to smoking, drinking and fear of visiting TB clinics were calculated, Chi square was test of significance used and  $p$ -value < 0.05 was considered significant. Table and bar graphs were the appropriate tools to present data.

### Results

In the 300 pulmonary tuberculosis patients enrolled, mean age was  $42.5 \pm 1$ , (median 42, IQR 13.5), diversity in ages can be explained due to hospital based data. Males were predominant 217 (72%), as compared to females 83 (28%). Majority belonged to lower socioeconomic status, 239 (79.7%) having an income < 25,000 compared to 61 (20.3%) with an income >25,000. About half of the participants and spouses were illiterate 154 (51.3%) and 161 (53.6%) respectively. Majority were self-employed 238 (79%) compared to government employed 28 (9%), unemployed 26 (9%) students 8 (3%).

Substantial stigmatization was being experienced by the participants within the society. In case of social factors, majority were not afraid to disclose disease to their families and others, 213 (71%) and 175 (58.3%) were not worried of being a burden on their family. On the contrary 158 (52.7%) felt hurt at the reaction of others on disclosing their disease. Many of them had lost their friends 216(72%) and more than half of them 152 (50.7%) were experiencing loneliness. Fear of visiting tuberculosis clinics was observed in 200 (67%) of the participants (Figure 1). They had no fear of being perceived as AIDS patients 235 (78.3%), no fear of developing AIDS 243 (81%) or Tuberculosis 190 (63.3%) due to smoking, drinking or other risky behaviors (Figure 2).

Significant relationships were observed between loneliness and losing friends after disclosure of Tuberculosis ( $p=0.000$ , CI=29.95-52.25). Participants were experiencing the feeling of being hurt after disclosure of Tuberculosis to people outside the family ( $p=0.000$ , CI=12.57-35.52), but had no fear of Tuberculosis being perceived as AIDS( $p=0.000$ , CI=8.58-32.36). Most of them had no fear of developing AIDS and experiencing loneliness which exhibited a significant relationship ( $p=0.01$ , CI=9.05-37.18).

### Discussion

Globally, Pakistan is included in countries having a high burden of Tuberculosis.<sup>21</sup> It is pertinent to assess stigmatizing attitudes towards tuberculous patients especially in countries like Pakistan

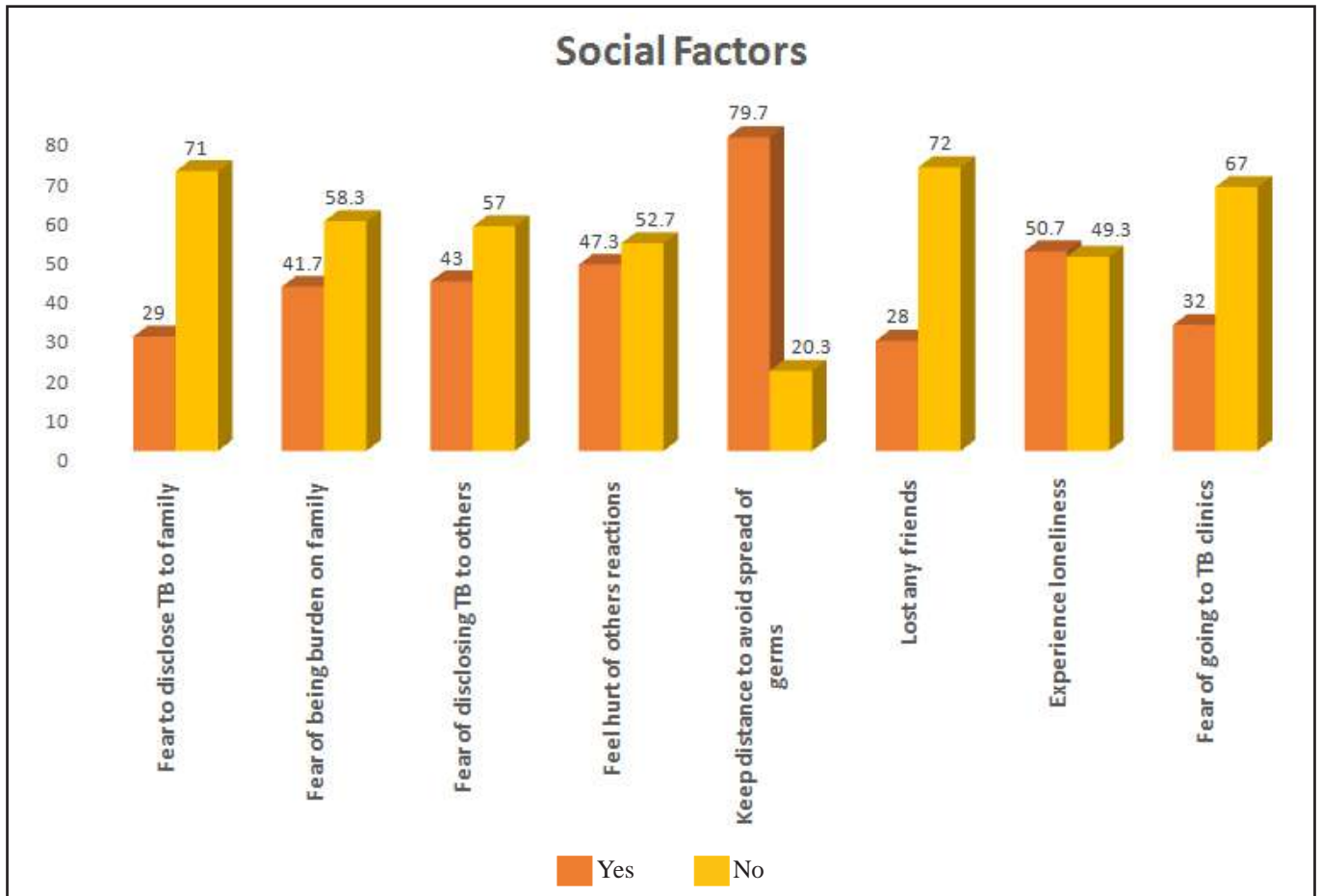


Fig 1. Social Factors associated with Stigma due to Tuberculosis

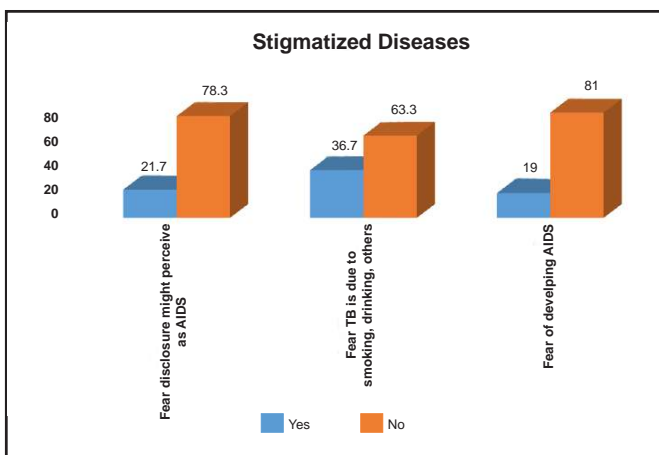


Fig 2. Stigmatized Diseases

where scarcity of studies is pronounced, in addition it also determines the health care seeking behavior of the patients. The current study evidenced male pre dominance (72%) supported by a study (70%) conducted in Thailand.<sup>22</sup> Middle

aged groups (25 – 46 years) were the major sufferers as discussed in the literature, mean age being 34 years. Poor educational status was a consistent finding, our study featuring majority of the participants and their spouses as illiterate (51–54%), concurrent with findings of Kipp.<sup>23</sup> Similarly another study states that literacy status was not associated with stigmatization against Tuberculosis.<sup>24</sup>

Minimal stigmatization against Tuberculosis within the family was observed in the current study, participants had no fear to disclose disease to their families (71%), contrary to the findings in literature, (23%) were not afraid of disclosing disease to their families.<sup>24</sup> In another study, participants stated that families never left them alone, thus they had no fears disclosing their disease to them.<sup>25</sup>

In another study it was evident that (51.3%) had a fear of disclosing disease to their families, (47.3%) felt hurt of others reactions to their disease, (41.7%) and were fearful of being a burden on their families which was attributed to their low socioeconomic status and productive age group.<sup>26</sup>

Loneliness the most painful aspect of stigmatization was

| Response | n (%)   | n (%)   | Confidence Interval | p value |
|----------|---|---|---------------------|---------|
|          | <b>Participants lost friends after disclosure of TB</b>                       | <b>Participants experiencing loneliness</b>                             |                     |         |
| Yes      | 84 (38.8)   | 68 (80.9)   | 29.95-52.24         | <0.001  |
| No       | 132 (61.1)  | 16 (19.0)   |                     |         |
|          | <b>Participants fear of disclosure of TB to people outside family</b>         | <b>Participants felt hurt of reaction of people on disclosure of TB</b> |                     |         |
| Yes      | 63 (36.8)   | 79 (61.2)   | 12.57-35.52         | <0.001  |
| No       | 108 (63.1)  | 50 (38.7)   |                     |         |
|          | <b>Participants fear of disclosure of TB outside the family</b>               | <b>Participants fear of disclosing TB as might be perceived as AIDS</b> |                     |         |
| Yes      | 32 (17.6)   | 33 (37.9)   | 8.58-32.26          | <0.001  |
| No       | 181 (84.9)  | 54 (62.0)   |                     |         |
|          | <b>Participants fear of developing AIDS</b>                                   | <b>Participants experience loneliness</b>                               |                     |         |
| Yes      | 112 (46.0)  | 40 (70.1)   | 9.05-37.18          | 0.01    |
| No       | 131 (53.9)  | 17 (29.8)   |                     |         |
|          | <b>Participants fear that TB developed due to smoking, drinking or others</b> | <b>Participants fear of developing AIDS</b>                             |                     |         |
| Yes      | 28 (49.1)   | 82 (33.7)   | 0.50-30.22          | 0.03    |
| No       | 29 (50.8)   | 161 (66.2)  |                     |         |

experienced by (50.7%) of the participants, although only (28%) had lost their friends after developing the disease ( $\chi^2$  42.811,  $p$ -value 0.000). Literature provides supporting evidence as various studies report that participants shared the experience of loneliness and isolation from families, communities and friends.<sup>25,26</sup> In a study conducted in India (98% ) patients were facing discriminating attitude.<sup>22</sup> On the contrary some studies factualize that patients have the support and encouragement of their friends, thus it helps reduce loneliness and isolation as was observed in the current study.<sup>22,23,27</sup> A pertinent observation was that patients were keeping a distance or avoiding coughing in front of people as to prevent spread of germs (79.7%), supported by another study in which (69.9%) patients were practicing the same.<sup>28</sup>

AIDS and Tuberculosis go hand in hand as far as stigmatization

is concerned. In the current study participants had minimal fears concerned with AIDS which may be attributed to illiteracy and low prevalence of HIV according to WHO in 2014, 68,000 people were reported to have HIV/AIDS in Pakistan.<sup>29</sup> In the current study the participants had minimal fear of TB being perceived as AIDS ( $\chi^2$  19.098,  $p$ -value 0.000) or fear of developing AIDS, (19%). A significant association was observed between fear of developing AIDS and experiencing loneliness ( $\chi^2$  10.715,  $p$ -value 0.01). Contrarily other studies reported stigma related to HIV (82%) and immoral behaviors as well as beliefs of patients that they had more chances of developing AIDS.<sup>28, 30</sup>

Smoking, drinking and many other activities can be attributed to Tuberculosis leading to misconceptions as quoted in a study, (34%) of the participants attributed their disease to smoking.<sup>31</sup>

In a study conducted in North Africa, (42%), smokers discontinued smoking and (41%) alcoholics discontinued drinking as they believed these activities were responsible for their disease.<sup>32</sup> But the current study negates these findings as (63.3%) did not attribute their disease to these factors and a significant relationship was exhibited between fear of developing TB due to smoking, drinking and fear of developing AIDS ( $\chi^2$  4.702,  $p$ -value 0.03).

Stigmatization leads to decrease in seeking healthcare and compliance of the patient. Studies have shown that due to fear of being stigmatized patients do not access health care facilities (46.2%),<sup>23</sup> contrary to the observations of the current study, (32%) were fearful of accessing Tuberculosis clinics. These results may be attributed to this study being hospital based.

### Conclusion

Stigmatization is an issue faced by many tuberculosis patients, the current study concludes that substantial stigmatization was being faced in the form of people having fears and experiences of loneliness and being left by friends depicted by a significant  $p$ -value. This is contributing to less health care seeking behavior and compliance of the patients which ultimately effects the overall control and spread of Tuberculosis, which is of high concern as Pakistan is high burden country for TB and we need to address and minimize this problem as much as possible. In countries like Pakistan strong family bonds and network are responsible for less stigmatization at family level.

### Recommendations

1. Patients and attendants visiting specialized Tuberculosis centers should be educated regarding stigmatization of patients and its implications on their treatment and mental status.
2. Families should be involved in accepting the disease by extensive counseling, as they play a major role being the support system for the sufferer and thus can increase compliance and reduce stigma not only at family level but at community level too.
3. Further researches should be conducted in other institutions and the community involving a larger sample, as we need to highlight this topic on various forums.

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## Antibiotic Resistance Pattern in Nosocomial Urinary Isolates of *Enterococcus*

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### Abstract

#### Background

Recent years have witnessed advancement in medical facilities and as a consequence increase in healthcare related infections. The leading problem in majority of hospitals is nosocomial infections. Among nosocomial infections UTI has utmost importance. *Enterococcus* is among one of nosocomial organisms. *Enterococcus* emerges as important nosocomial pathogen during past few decades. The present research project was designed to study drug susceptibility of clinical isolates of *Enterococcus* species to have better knowledge in understanding the emerging organism and making treatment more accurate.

#### Results

52.72% (29) were isolated from urine samples collected from female patients whereas 47.27% (26) from male patients. *Enterococcus faecalis* was present in 87.27% (48) clinical cases and *Enterococcus faecium* in 12.7% (07). *Enterococcus* was frequently isolated from medicine 42% (23) and ICU 29% (16) wards. In this study, Quinolones group showed high resistance where as fosfomycin, vancomycin and linezolid were found useful against *Enterococcus* infections.

#### Methods

55 positive culture of *Enterococcus* were analyzed after collection of urine sample from different hospitals. Urine samples were streaked on CLED medium for isolation of organisms. Organisms were identified by their colonial characteristics and gram staining. For further identification bile esculin test and mannitol salt agar test was performed.

#### Conclusion

*Enterococcus* is emerging as important nosocomial uropathogen. Antibiotic resistance among *Enterococci* spp. are on rise and become great concern for hospital setup. Quinolones prescription should be eluded as empirical treatment for *Enterococcus* urinary tract infection whereas fosfomycin, Vancomycin and linezolid are potent drugs but should be used with caution.

#### Key words

Urinary tract infection, *Enterococcus*, Nosocomial infection or

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hospital acquired infection, antimicrobial susceptibility.

#### Introduction

Past decades have witnessed great progress in medical field. Currently, increase in invasive and complicated procedures lead to increase in opportunistic infections.<sup>1</sup> Nosocomial or hospital acquired infections (HAI) are those infections which are acquired by patient during hospital stay. HAIs are considered continuous threat and extra burden to patient and health authorities.<sup>2</sup> Among hospital acquired infections urinary tract infection are a frequent cause. About 40% of all nosocomial infections are urinary tract infection.<sup>3</sup> The financial implication and morbidity and mortality related to these infections are major problem for hospital resources.

Approximately 80% of nosocomial UTIs are related to urinary catheterization.<sup>3</sup> However, old age, diabetes mellitus, renal diseases, any debilitating disease and other several factors are associated with UTIs. Even hospital-acquired urinary tract infections can lead to urosepsis and septic shock. The ultimate treatment of these infections is antibiotic but the irrational use of antibiotics especially in Pakistan has contributed significantly in development of drug resistance and evolution of multidrug resistance strains. Nosocomial uropathogens show more antibiotic resistance than community acquired UTIs.<sup>3</sup> This trend can be seen in isolated strains of *Enterococcus* from clinical samples.

*Enterococci* are gram positive organisms that are part of normal gut micro-biota. Over the last few decades *Enterococcus* emerge as important health care associated pathogen due to their potential to withstand extreme and harsh circumstances. In addition, intrinsic and increasing acquired resistance among *Enterococcus* isolates to many antibiotics also creating challenges for health-providing authorities.<sup>4</sup>

*E. faecalis* and *E. faecium*, are among the main pathogenic strains. *Enterococcus* is involved in serious nosocomial infections such as urinary tract infection. But the organism can cause other diseases like endocarditis, bacteremia, sepsis and rarely meningitis.<sup>5,6</sup> The contributing factors for *Enterococcus* infection include catheterization, impaired host immunity, use of antibiotics, old age etc.

The ability to resist multiple antibiotics makes *Enterococcus*

a real threat. *Enterococcus* exhibits intrinsic and acquired resistance. The intrinsic resistance is present in all *Enterococcus* species. *Enterococci* are intrinsically resistant to tetracycline, trimethoprim-sulfamethoxazole, aminoglycosides and cephalosporins. These are empirically prescribed antibiotics to cure Urinary tract infections and *Enterococcus* infection. By acquiring antimicrobial resistance, *Enterococci* can survive for more period of time. The indiscriminate use of antibiotics allows *Enterococci* to develop acquired resistance against different classes of antibiotics which include glycopeptides, tetracycline, chloramphenicol, nitrofurantoin and quinolones.

The substantial rise in antibiotic resistance of *Enterococcus* species across the world emphasizes on the better understanding of this organism. Infection control programs and policies are imperative in minimizing the chance of hospital-acquired UTIs. Knowledge of *Enterococcus* resistance pattern is essential for treatment purpose. This would be helpful in determining the importance of *Enterococcus* infection.

#### Materials and Methods

In present study urine samples were collected from Civil hospital Karachi and Zubaida Medical Centre, Karachi during a period from December 2014 to March 2016 and analyzed. Midstream urine samples were collected from patients suffering from acute or chronic urinary tract infection, catheterized or uncatheterized, school going children, young and grownup adults of either sex while menstruating women, toddlers, infants and those having renal, bladder and genital tumors were not included.

From uncatheterized patients samples were collected in a properly labeled sterile plastic container whereas in catheterized patients urine sample were taken from part of catheter after taking consent from patient/attendant after sample collection, samples were analyzed within 6 hours. Urine samples were streaked on Cysteine Lactose Electrolyte Deficient (CLED) (Oxoid) agar. Urine sample was considered positive by presence of bacterial count 1000-10,000cfu/ml.<sup>7</sup> Colonies were examined and identified on the presence of peculiar colony characteristics and further identified by gram staining and catalase test. Bile esculin test and mannitol salt agar test were performed for further identification of *Enterococcus* spp.

The susceptibility of *Enterococcus* spp. to empirically used antibiotics against urinary tract infection was tested by using Kirby-Bauer disc diffusion method<sup>8</sup> and interpreted in reference to CLSI.<sup>9</sup> Bacterial suspension was prepared to match the standard 0.5 McFarland index. Sterile cotton swab was used to prepare bacterial lawn on Mueller-Hinton agar plates (Oxoid) in three different directions to obtain a uniform inoculum over the entire plate. Antibiotic discs were placed on medium with the help of forceps. Antibiotic discs of different concentration were used. These include: imipenem(10µg), ampicillin (10µg), piperacillin (100µg), levofloxacin (5µg), norfloxacin (10µg), nalidixic acid (30µg), piperimidic acid (20µg), fosfomycin (50µg),

Vancomycin (30µg) and linezolid (30µg) and co-amoxiclav (20/10)µg (Oxoid). Plates were examined after 24 hours of incubation at 37°C and cleared areas around discs were measured and noted in mm. *E. faecalis* ATCC 29212 was used as reference strain for antibiotic susceptibility testing.

#### Results

In total 55 urine samples showing positive growth of *Enterococcus* spp. were analyzed. Out of 55 *Enterococcus* isolates, 42% (n=23) strains were isolated from medicine ward followed by ICU 29% (n=16) and gynecological ward 14% (n=8) (Fig 1), among which 53% (n=29) were isolated from urine samples of female patients whereas 47% (n=26) were from male patients (Fig 2). *Enterococcus faecalis* was present in 87% (n=48) samples and *Enterococcus faecium* in 13% (n=7) (Fig 2). The age of patient ranged between 5-90 years. The median age was 40 years.

#### Antibiotic Resistance Patterns in *E. faecalis* and *E. faecium*

The drug susceptibility of *Enterococcus* against different antimicrobials was showed in table (Table 1). High resistance against quinolones was observed in *E. faecalis* isolated from oncology, ICU and surgical ward (88%, 84% and 80% respectively) (Fig 3). *E. faecium* (64%) were observed resistant to beta lactam drugs isolated from various wards of hospital. Vancomycin resistant was noticed particularly in *E. faecalis* isolated from ICU ward. 29% VRE were isolated from ICU and gynecological ward preceded by 15% in medicine.

#### Discussion

Recently *Enterococcus* has emerged as multifaceted and important nosocomial uropathogen.<sup>1,10</sup> As antimicrobial resistance is high among *Enterococcus* species, it is wise to find out the sources to control *Enterococcus* infections. Kahlmeter (2003)<sup>11</sup> found *Enterococci* amongst the leading cause of UTI in hospitals.

In recent study prevalence of *Enterococcus* spp. were mainly

#### Number of Organisms Isolated from Different Wards of Hospital

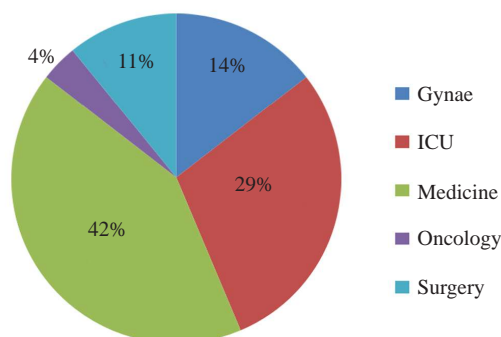
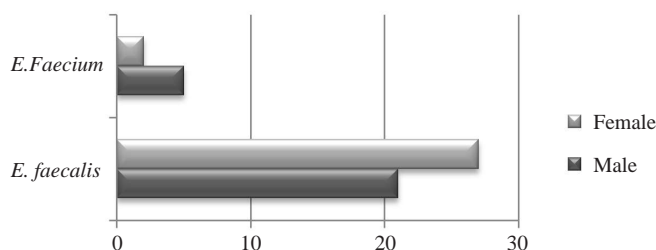


Fig 1. Frequency of *Enterococcus* spp collected from different wards of hospitals



**Fig 2. Gender and Age wise distribution of *E. faecalis* and *E. faecium***

**Table 1: Antimicrobial susceptibility of *Enterococcus* spp.**

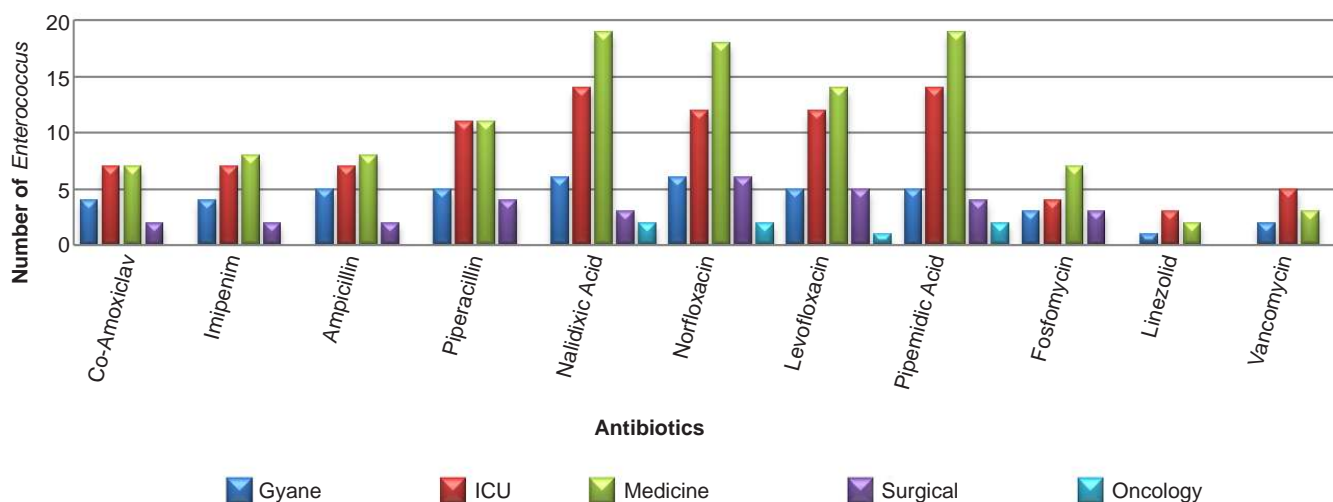
| Antimicrobial disc (Oxoid) | Susceptible | Inter-mediate | Resistant  |
|----------------------------|-------------|---------------|------------|
| Linezolid(30µg)            | 49 (89%)    | -             | 06 (11%)   |
| Vancomycin(30µg)           | 43 (78%)    | 2(4%)         | 10 (18%)   |
| Fosfomycin(50µg)           | 38(69%)     | -             | 17(31%)    |
| Co-amoxiclav(20\10µg)      | 35(64%)     | -             | 20 (36%)   |
| Imipenem(10µg)             | 34(62%)     | -             | 21(38%)    |
| Ampicillin(10µg)           | 33(60%)     | -             | 22(40%)    |
| Piperacillin(100µg)        | 24 (43.6%)  | -             | 31(56.36%) |
| Levofloxacin(5µg)          | 17 (31%)    | 1(2%)         | 37(67%)    |
| Norflaxacin(10µg)          | 11(20%)     | -             | 44(80%)    |
| Nalidixic acid(30µg)       | 11(20%)     | -             | 44(80%)    |
| Pipedemic acid(20µg)       | 11(20%)     | -             | 44(80%)    |

observed in urine samples collected from medicine ward followed by ICU. Majority of patients admitted to these wards via emergency department suffered from chronic or acute illness. These patients may require catheterization, complex invasive procedures and antibiotics administration more frequently as compared to patients admitted via OPD. In US approximately 5% catheterized patients develop urinary tract infections.<sup>12</sup> In addition, excessive antibiotics administration disturb normal flora hence more chances of infection. In China, a study conducted in a hospital showed that *Enterococcus* was mainly isolated from burns center.<sup>1</sup> In another study by Richards and his colleagues (2000)<sup>13</sup> revealed 20-30% UTIs in ICU wards.

In present study *E. faecalis* was one of the important uropathogen isolated from catheterized patients. Pascale *et al.*, (2013)<sup>14</sup> demonstrated *E. faecalis* as main pathogen in catheterized patients. In another study in Mexico *E. faecalis* and *E. faecium* was found to be 81.2%. However Salem-Bekhit (2012)<sup>15</sup> and partners reported 69% *E. faecalis* and 11% *E. faecium* isolates from clinical samples in hospital in Saudi Arabia.

High antibiotic resistance among *Enterococcus* species is probably due to easy survival of these organisms in extreme conditions. Quinolones are frequently prescribed medicine for treatment of urinary, respiratory, and gastrointestinal tract infections.<sup>16</sup> Current study revealed high resistance against quinolones (nalidixic acid, piperidic acid and norfloxacin). About 80% *Enterococcus* isolates showed resistance against quinolones. Altaf and Tuba (2015)<sup>17</sup> came across with similar observations. Variation in quinolones resistance can be observed across the world depending on various factors. An Indian study demonstrated 75% quinolones resistance,<sup>18</sup> UK, Australia and France, showed low resistance rate.<sup>17</sup> This happens due to

**Number of Resistant *Enterococcus* in Different Wards**



**Fig 3. Numbers of resistant *Enterococcus* spp isolated from different wards**

discipline in prescribing and controlled sale of antimicrobials. Rattanaumpawan *et al*, (2011)<sup>19</sup> described that quinolones resistance in *Enterococcus* was particularly noticed who were subsequently exposed to clindamycin, cephalosporin and flouroquinolones.

The resistance pattern of beta lactam drugs; imipenim, ampicillin, piperacillin and amoxiclav against *Enterococcus* was observed. Because of low affinity of penicillin binding proteins, the effectiveness of  $\beta$ -lactam drugs has been reduced among gram positive *Enterococci*.<sup>20</sup> In this study 64.28% isolated *E. faecium* were found resistant to  $\beta$ -lactams drugs. These results are in close association with Wei *et al* (2014).<sup>1</sup> However in another study Shamshad *et al* (2014)<sup>21</sup> demonstrated 25%, 12% and 8% resistant isolates against ampicillin, co-amoxiclav and imipenem, respectively. Farhan and his colleagues (2006)<sup>22</sup> observed 45% ampicillin resistant isolates.

Vancomycin aglycopeptides was introduced due to resistance in other drugs. Vancomycin resistance was first observed in *Enterococcus* and afterwards in *S. aureus*.<sup>23</sup> In present study 18% VRE strains were isolated from urine samples. These results are very much similar to Asif *et al* (2014)<sup>24</sup> in Lahore (Pakistan) revealed 16.2% VRE. However, 3% Vancomycin resistance was observed by Shamshad *et al.*, (2014).<sup>21</sup> Farhan and Essa, (2006)<sup>22</sup> and The Laboratory, Karachi, demonstrated only one% VRE. However Vancomycin resistance vary considerably.<sup>25</sup> In accordance with CDC, in US 30% Vancomycin resistant strains were observed while in a Brazilian, Iran and Indian tertiary hospital VRE observed 15.5%, 20.5% and 12% respectively.<sup>26</sup> Literature survey also pointed towards transferring of resistant gene to other organisms via VRE.<sup>27</sup> Beyond all, Vancomycin is still considered as better treatment option for *Enterococcus* infection.

In present study antibiotic resistance in different hospital's ward varied. Quinolones resistance was mainly observed in strains, isolated from urine samples collected from medicine unit. This may be attributed to condition of patient, depressed immunity and prolonged use of antibiotic. Prevalence of beta lactam resistance was observed mainly in isolates collected from gynaecological ward. In another study by Shah (2004)<sup>28</sup>, use of ampicillin and co-amoxiclav was studied. He reported that maximum numbers of antibiotics were given for LSCS. In our hospitals drastic increase in LSCS without proper indications is important contributing factor. In recent study VRE strains were mainly isolated from ICU ward. VRE ranks second among resistant organisms in ICU patients.<sup>29</sup>

## Conclusion

Due to presence of drug resistance, *Enterococcus* treatment become challenging as fewer options are available. For betterment antibiotic should be selected after culture and susceptibility and narrow spectrum antibiotic should be preferred. With limited health resources, a policy should be

constructed for resistant strains.

## Authors Contribution

Aqeel Ahmad (Help in study design, planning, analysis, interpretation, discussion, facilitated for reagents, critical review); Ghulam Fatima (facilitated for reagents, critical review); Sabiha Mirza (facilitated for reagents, critical review) and Mehveen Iqbal (Concept, study design, study conductor, analysis, interpretation, discussion, manuscript writing, finalize research paper).

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## Health Related Quality of Life among People Living with HIV /AIDS in Pakistan

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### Abstract

#### Objective

To assess quality of life in HIV /AIDS patients on Anti-retroviral therapy using WHO QOL- BREF instrument.

#### Study design

Cross sectional study.

#### Place and duration of study

The study was conducted in outpatient department of The Indus Hospital, Karachi from January to July 2016.

#### Methodology

Quality of life (QOL) was evaluated using the WHO QOL BREF instrument (translated Urdu version) using 31 items grouped under 6 domains: namely physical, psychological, level of dependence, social relations, environment and spirituality.

The demographics along with CD<sub>4</sub> counts, stage of disease and viral loads and duration of Anti-retroviral therapy were recorded. It was a cross sectional study and sample size was 109 patients. Data was entered and analyzed using SPSS version 21.0. The equation suggested by WHO was applied to overall estimation of each domain with scores ranging from 4 to 20.

#### Results

A total of 109 participants completed the questionnaire out of which 76 (69.7%) were males, 28 (25.7%) were females and 3 (1.8%) were transgender. Mean (SD) age of patients was 39.2 (10.9) years. Regarding marital status 77(70.6%) were married, 20(18.3%) were single, 4(3.7%) were divorced and 7(6.4%) were widowed. Majority 94 (86.2%) had revealed their sero-status to their relatives and 8 (7.3%) did not reveal their illness 99 (90.8%) were in stage 1 of AIDS, 5 (4.6%) were in stage 2, 1 (0.9%) were in stage 3 and 4 respectively. Majority of patients were illiterate comprising 36 (33%), 21(19.3%) had primary/middle education, 18(16.5%) had degree graduation and above. Regarding marital status 77(70.6%) were married, 20(18.3%) were single, 4(3.7%) were divorced and 7 (6.4%) were widowed. Highest scores were noted in domains of physical health, spiritual, and religious beliefs. (Median scores 15 in

both). Psychological domain scored average, social relations and environment were the two domains in which low scores were noted as compared to other domains. Overall the quality of life of the patients was found to be fair to average. (Mean score: 13.7).

#### Conclusion

Our study WHO-QOL BREF instrument Urdu version showed that QOL scores were high in physical health, spirituality/religious domains, fair scores were obtained in psychological domains whereas social relations, and environmental aspects scored less.

#### Key words

WHO QOL BREF, HIV, and AIDS.

#### Introduction

HIV/AIDS pandemic has affected different aspects of a society involving individuals, families, sectors and institutions. It has distorted and ruined the social framework of many communities and countries, especially the heavily infected ones.<sup>1</sup>

The estimated global number of people living with HIV (PLHIV) including adults and children at the end of 2009 was 33.3 million. The majority is in Sub-Saharan Africa which is estimated at 22.5 million, but there is a rising trend in the epidemic in Asia and Eastern Europe. New HIV infection worldwide is estimated to be 2.6 million and the number of death due to AIDS defining illness was 1.8 million in the year 2009.<sup>1</sup>

Although initially Pakistan was depicted as a country free of HIV, first case was reported in 1986 and since then the number of HIV patients is rising gradually but steadily.

As per Asian Pacific Model Asian countries with rampant HIV spread, Pakistan ranks fourth, others are Indonesia, Malaysia and Philippines.<sup>11</sup> In these countries the HIV epidemic is spreading with high new cases being reported each year as compared to the previous year, in 2014 roughly 15606 cases were reported as new cases.<sup>11</sup>

According to the statistical analysis of Asian Epidemic Modelling (AEM), conducted in 2015, use of contaminated injections among people who inject drugs (PWID) remains the main mode of HIV transmission in the Pakistan. Due to advances in Anti-retroviral therapy (ARV) there has occurred marked improvement

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in life expectancy and quality of life in patients with HIV infection.

ARV was introduced in Pakistan in 2006 through National AIDS Control Program. The Indus Hospital is one of the sub recipients of ARV, and has been providing consultation, counseling, lab tests and ARV completely free of charge. Patients are referred to the AIDS clinic through physicians, self-referral or through friends or family members. The initial phase of denial, anger, anxiety, guilt and depression are gradually replaced with acceptance. As patients' clinical symptoms improve on ARV, and follow up at the clinics, it is expected that they will return to their normal lives. However quality of life remains a paramount issue.

WHO has defined QOL as the individual's perception of their position in life in the context of culture and value system in which they live, and in relation to their goals, expectations, standards and concerns.<sup>2</sup> QOL is a newly developed, multidimensional, generic cross cultural instrument developed for use across patients groups in various countries.<sup>9</sup> It applies to many chronic diseases such as tuberculosis, diabetes, heart disease, etc. It is now a cost effective and essential tool for analysis of HIV disease as well.<sup>3</sup> HRQOL gives an insight on the quality of health care system.<sup>3</sup>

In an era of advanced Anti Retro Virals (ARV) the life expectancy of HIV /AIDS patient has increased, highlighting the importance psychosocial aspect in quality of life in such patients.<sup>12</sup>

Other than the disease process, such patients suffer a decline in quality of life due to multiple factors like addictions, poverty, social stigma, depression and violence, which adversely affects the disease process and causes poor outcomes.<sup>12</sup>

The WHOQOL-BREF was developed as a cross cultural instrument whose contents are easily applicable to different cultures worldwide.<sup>12</sup>

This is a multi-faceted generic profile which includes 31 items covering six main domains including physical, psychological, level of independence, social relationships, environment and spirituality. The physical health domain consisted of seven items, including impact of disease on daily activities, medicinal dependence, fatigue, presence of pain discomfort restricted mobility, sleep and rest, lack of energy and initiative and working ability.

The psychological well-being domain included eight items assessing patient's thoughts about body image, appearance, positive and negative feelings, self-esteem and personal beliefs, higher cognitive functions, anxiety, suicide, depression.

Third domain was social relationships consisting of three items that assesses personal relationships, social support and sexuality.

Environmental domain has eight facets like home environment,

financial resources, physical safety security, health social care transport, physical environment, opportunity for leisure activities, acquiring new information and skills. Spiritual, personal and religious belief domain has four aspects like forgiveness, blame, personal belief, death /dying and concern about the future.

### **Methodology**

It was a cross sectional survey of patients living with HIV/AIDS visiting the Infectious Diseases outpatient department of The Indus Hospital Karachi. The duration of study was six months from January till June 2016.

The participants were explained the purpose of the study and potential benefits, confidentiality was ensured, written consent was taken and the patients were given the questionnaire. The World Health Organization Quality of life HIV BREF Instrument (WHO QOL-HIV BREF Urdu questionnaire Urdu version) was used. It was reviewed by expert members of Institutional Review Board, and Ethical approval was obtained.

For analysis the following factors were evaluated as independent variables like age, gender, marital status (married, single, widowed and divorced), level of education (illiterate, elementary, diploma and university degree), income along with work status, CD<sub>4</sub> counts, stage of disease and viral loads and duration of Anti-retroviral therapy.

The questionnaire consisted of six domain comprising 31 questions; it was designed to assess quality of life of participant in terms of individual's perception of their life in context of physical health, level of dependence, spiritual, social, financial and psychological aspect. Participants answered each question using a 5 item Likert scale where 1 shows low and negative perceptions and 5 indicates high and positive perceptions. Facet scores were calculated as means of their items scores and range between 1 and 5. Patients who were educated filled the questionnaire themselves and those who were uneducated or too ill to fill the form were helped by us.

Inclusion criteria were HIV/AIDS positive registered patients at the Indus Hospital, those on ARV for at least six months, age above 18 years and willing participants.

The patients who were excluded from study were terminally ill or newly diagnosed patients, and unwilling participants.

Data was entered and analyzed using SPSS version 21.0. The equation suggested by WHO was applied to overall estimation of each domain with scores ranging from 4 to 20. Independent sample T-test/ Mann-Whitney U test was applied to assess significant difference in overall scores and scores of each domain between both the genders. ANOVA/Kruskal Wallis test was applied to assess significant differences in scores among marital status, education level and age groups. For easy and better interpretation of results, scores were categorized as low

level (between 4 and 10), intermediate scores (between 10 and 14.9) and high scores (between 15 and 20). Chi-square/Fisher-exact/Likelihood ratio chi-square test were applied as appropriate to find association of gender, education level, marital status and age groups with score categories of different domains. *P*-value <0.05 were considered significant.

### Results

A total of 109 participants completed the questionnaire out of which 76 (69.7%) were males, 28 (25.7%) were females and 3 (1.8%) were transgender. Mean (SD) age of patients was 39.2 (10.9) years. Regarding marital status 77(70.6%) were married, 20(18.3%) were single, 4(3.7%) were divorced and 7(6.4%) were widowed. Majority 94 (86.2%) had revealed their serostatus to their relatives and 8 (7.3%) did not reveal their illness Table (1).

99 (90.8%) were in stage 1 of AIDS, 5 (4.6%) were in stage 2, 1 (0.9%) were in stage 3 and 4 respectively.

Highest scores were noted in domains of physical health, spiritual, and religious beliefs. (Median scores 15 in both). Psychological domain scored average, social relations and environment were the two domains in which low scores were noted as compared to other domains. Overall the quality of life of the patients was found to be fair to average. (Mean score: 13.7) Table (2).

**Table 1: Sociodemographic characteristics of the participants.**

| Variables                             | Frequency (%)     |            |
|---------------------------------------|-------------------|------------|
| Gender                                | Male              | 76(69.7)   |
|                                       | Female            | 28 (25.7)  |
|                                       | Transgender       | 2 (1.8 )   |
| Mean age in years ± SD                | 39.2 years        |            |
| Marital status                        | Married           | 77 (70.6 ) |
|                                       | Single            | 20 (18.3)  |
|                                       | Widow             | 7(6.4)     |
|                                       | Divorced          | 4(3.7)     |
| Education                             | Illiterate        | 21(19.3)   |
|                                       | Primary/middle    | 20(18.3)   |
|                                       | College and above | 18(16.5)   |
| Friends knowing serostatus of patient | Yes               | 94(86.2)   |
|                                       | No                | 8(7.3)     |
| Stage of HIV infection                | Stage 1           | 99(90.8)   |
|                                       | Stage 2           | 5(4.6)     |
|                                       | Stage 3           | 1(0.9)     |

**Table 2: Mean scores for quality of life in six domains of WHO QOL (N=109)**

| WHO QOL Domain                                       | Mean SD | Median IQR                  | Min-Max |
|--|---------|-----------------------------|---------|
| Physical Health <sup>a</sup>                         | 109     | 14.8(3.1)<br>15 (13-7)      | 6-20    |
| Psychological  | 109     | 14.1(2.9)<br>4.4 (12-16)    | 6.4-20  |
| Level of Independence <sup>a</sup>                   | 109     | 13.9(3.1)<br>14 (12 16)     | 5-20    |
| Social Relations <sup>a</sup>                        | 109     | 12.9(3.9)<br>13 (10-16)     | 5-20    |
| Environment  | 109     | 12.7(3)<br>12.5 (11-14.5)   | 5-20    |
| Spiritual / Religion / Personal Beliefs <sup>a</sup> | 109     | 14.8(3.2)<br>15 (12-17)     | 5-20    |
| Overall  | 109     | 13.7(2.8)<br>14 (11.6-15.6) | 7-20    |
| Overall  | 109     |                             | 7.3-20  |

Majority of patients were illiterate comprising 36 (33 %), 21(19.3%) had primary/middle education, 18(16.5%) had degree graduation and above. Regarding marital status 77(70.6%) were married, 20(18.3%) were single, 4( 3.7%) were divorced and 7 (6.4%) were widowed.

Statistically significant difference was observed in physical health and social relations scores between both the genders (*P*-value: 0.041 and 0.049 respectively). Males were found to have higher scores in these two domains as compared to females (Median scores: 16 vs 14; 13 vs 12; respectively). However, in the remaining domains both males and females had approximately similar scores. Overall, males were found to have better health than females, but result was not statistically significant (Mean overall scores: 14.4 vs. 12.9, *P*-value: 0.127) Table (3).

No statistically significant difference was observed in scores of any WHO QoL domain among marital status.

### Discussion

In our study highest QOL scores were obtained in domains of physical health and religious beliefs. It showed that majority of patients compliant on anti-retroviral therapy enjoyed a satisfactory physical health, they had minimal medicinal dependence for body aches and pain, enjoyed good sleep and had a positive outlook towards life. Spirituality and social



**Table 3: Showing gender based WHO QOL domain scores.**

| WHO QoL domains' score                     | Gender |                              |        |                                | P-value |
|--|--------|------------------------------|--------|--------------------------------|---------|
|  | Male   |                              | Female |                                |         |
|  | n      | Mean (SD)<br>Median (IQR)    | n      | Mean (SD)<br>Median (IQR)      |         |
| Physical health                            | 76     | 15.1 (3.4)<br>16 (13-18)     | 28     | 14.2 (2.5)<br>14 (12-16)       | 0.041*† |
| Psychological                              | 76     | 14.3 (3)<br>14.4 (12-16.6)   | 28     | 13.8 (2.8)<br>14 (11.4-15.2)   | 0.479‡  |
| Level of Independence                      | 76     | 14.1 (3.1)<br>14.5 (13-16)   | 28     | 13.6 (2.9)<br>14 (11-16)       | 0.523‡  |
| Social Relations                           | 73     | 13.5 (3.9)<br>13 (10.5-16)   | 28     | 11.7 (3.7)<br>12 (8.2-13.8)    | 0.049*† |
| Environment                                | 75     | 12.8 (3.1)<br>12.5 (11-14.5) | 27     | 12.4 (3.1)<br>12.5 (11-13.5)   | 0.477‡  |
| Spiritual / Religion /<br>Personal Beliefs | 76     | 15.1 (3.2)<br>16 (12.25-18)  | 26     | 14.3 (3.1)<br>14.5 (11-17)     | 0.218†  |
| Overall scores                             | 76     | 14 (2.9)<br>14.4 (11.8-15.8) | 28     | 13.1 (2.6)<br>12.9 (10.9-14.9) | 0.127‡  |

\*P-value<0.05, \*\*p-value<0.0001, ‡Independent sample T-test; † Mann-Whitney U test

support system may influence survival in patients with chronic, life threatening illnesses.<sup>10</sup> Spirituality and religion is a significant yet an overtly neglected facet of quality of life in patients with chronic, debilitating and stigmatizing diseases like HIV /AIDS.<sup>12</sup>

A high scoring QOL was related with drug adherence along with strong spiritual/religious beliefs leading to optimistic approach for future and positive self-perception. It is also believed that addressing spiritual needs of a patient may serve to decrease depressive symptoms.<sup>7,12</sup>

Psychologically our patients scored well, majority of the patients had an optimistic approach towards life, had intact cognitive functions which helped them to cope up with the challenges of daily life. They had minimal to nonexistent suicidal tendencies and had an energetic and hopeful approach towards future.

Social relations and environmental domains were the two domains scoring less, the reasons being multi factorial such as illiteracy, poverty, scarcity of robust health care system, lack of leisure activities, limited resources for acquiring new

information and an unsatisfactory transport system as many patients were coming from far flung areas of Pakistan. High degree of stigmatization hindered opportunities for better job prospects.

Social relations domain also scored low. Majority of patients had poor interpersonal and sexual relations and especially the female patients who got infected from husbands often had resentment, guilt and negative emotions. Males comparatively had better scores in physical health and social relations as compared to females.

Overall males enjoyed a better health as compared to females but it was not statistically significant. Surprisingly, marital status, CD<sub>4</sub>count, income did not have a statistically significant impact on over all QOL. Majority of patients were virally suppressed and immunologically stable.

**Study limitations**

The present study had some limitations like small sample size (109) and especially less number of female patients. Most importantly the participants were selected on hospital based

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consultations therefore due to convenient sampling method the instrument could not be used in community level causing a bias in results. As such the result of study is not a depiction of all HIV/AIDS patients in Pakistan.

### Conclusion

In brief our study WHO-QOL BREF instrument Urdu version proved to be a useful convenient and cost effective method for assessing quality of life in HIV / AIDS patients.

It further showed that QOL scores were high in physical health, spirituality/religious domains, fair scores were obtained in psychological domains whereas social relations, and environmental aspects scored less. The Indus Hospital Karachi has an integrated and programmatic approach towards patient management involving qualified clinicians, well trained counselors, paramedical staff, rehabilitation centers and uninterrupted medicinal supply by (Sindh Aids Control Programme). This collaborated approach thus has significant impact on QOL of our patients.

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## Post Dengue Infectious Syndrome

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### Abstract

We are sharing here a rare condition in a patient who had persistent debilitating systemic symptoms after resolution of acute dengue fever. A 35y/o male patient was diagnosed with post dengue infectious syndrome after other autoimmune etiologies were ruled out. Our patient was treated symptomatically and improved after four months.

### Introduction

Post Dengue Infectious Syndrome refers to the continuation of a broad range of symptoms after resolution of acute phase of Dengue Fever.<sup>1</sup> Seet *et al* conducted a study on 163 patients with dengue and found that 31(24.4%) of them went on to develop severe fatigue 2 months post acute phase of the infection.<sup>1</sup> The condition results from reduced clearance of antigen antibody complexes and resultant altered immune regulation in predisposed individuals.<sup>3</sup> The management is primarily symptomatic. To the best of our knowledge it is a rare condition and there is not enough literature regarding its prognosis. We are reporting a case of Post Dengue Infectious Syndrome whose symptoms resolve after 4 months. The only known prevention of this syndrome is to prevent the acute dengue viral infection which is a mosquito borne illness in endemic areas.

### Case:

A 35 years old male with no significant past medical history presented with high grade fever, increased frequency of urination, nausea and body aches since 3 days. Clinical examination showed a heavy built man, clinically stable but in physical discomfort having a generalized erythematous maculopapular blanchable rash. Blood work showed reduced platelets of 87,000, Dengue NS1 antigen positive, negative for dengue IgM and positive for Dengue IgG and moderately raised transaminases. Thus, our patient was diagnosed with an acute episode of dengue viral fever with antigen testing reported positive. This was considered to be a secondary infection as his dengue IgG was positive as well.

He was hydrated and temperature was monitored. Subsequently developed phlebitis at the cannula site and blood cultures

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returned positive for *Aeromonas spp*. We suspected contamination during handling of the cannula as the cause of aeromonas bacteremia, which occurs commonly following phlebitis in our hospital setting. He was started on ciprofloxacin based on culture and sensitivity.

His platelets dropped further to 34000 before improving, however his fever continued although lower grade. He completed 7 days of ciprofloxacin and platelet recovered gradually. His blood culture was repeated which showed no growth and he was discharged home.

After 2 weeks he came back with fever spikes 101- 102<sup>0</sup>F, dizziness, back ache and increasing weakness and lethargy so much so that he was unable to join his work. His labs were normal, CRP was 0.7 (normal value 1-3mg/L) and ESR was 67. A CT scan was performed to rule out occult infection and was unremarkable. This was followed by an echocardiogram without any significant findings. Autoimmune profile was negative for ANA.

We evaluated him for mental and physical fatigue using the Fatigue Questionnaire, a validated questionnaire used to assess patient functionality in various medical disorders. He scored moderate to severe on questions encompassing physical fatigue including problems with tiredness, difficulty initiating tasks, lack of energy and muscle strength. He scored mild on the mental fatigue questions relating to increased drowsiness and inability to think clearly. His overall score was 20 out of 30 on the questionnaire putting him in the moderate-severe category. Patient continued to report low grade fevers, continued dizziness and weakness over the course of several weeks despite all tests remaining negative. We subsequently diagnosed him with post infectious Dengue Syndrome.

We provided our patient with symptomatic relief with analgesics. His symptoms resolved gradually over 4-5 months and he eventually made complete recovery without any residual deficits.

### Discussion

Post Dengue Fatigue Syndrome is the persistence of a variety of disabling symptoms after resolution of the acute phase. The factors implicated are "host" related that predispose some individuals to an atypical immune response resulting in persistent symptoms.<sup>1</sup> Common clinical sequelae of post dengue infectious syndrome include arthralgia, asthenia, hand weakness, malaise, irritability, memory loss, dizziness, palpitations, headache, anorexia, alopecia, rash, nausea and diarrhea. Of these symptoms,

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arthralgia is reported to be most common.<sup>2</sup>

It is common within the first two years' post-acute infection. Studies indicate that the severity of acute infection itself correlates rather poorly to the development of the post infectious syndrome.

The pathology behind the abnormal immune response is thought to be related to abnormal binding property of the Fc portion of IgG in individuals with allelic variance. Individuals with the variant allele have abnormally low antibody affinity for antigen and therefore have reduced clearing of the antigen antibody complexes.<sup>3</sup>

Pathways of increased cytokines, TNF, interferon and interleukins are further stimulated due to abnormal regulation of macrophages, neutrophils and dendritic cells by the circulating antigen antibody complexes. These complexes persist in circulation and get deposited in various organs resulting in continued inflammation. The resultant clinical presentation is continued pain in muscles and joints.<sup>4</sup>

Laboratory tests that can aid in diagnosis include IgG titers and other autoimmune markers such as CRP, immune complexes and ANA. These findings are supportive of a disturbance in immune regulation resulting in increased production of cytokines and damage to the organs and tissues where immune complexes are deposited as well as the endothelial cells.<sup>2</sup>

There are few case reports available, however, a prospective study conducted in Singapore in 2005 identified 25 percent of patients with dengue who went on to develop persistent symptoms 2 months post the acute dengue episode. It related female sex, older age, presence of chills and absence of rash as factors that increase predisposition to persistent symptoms after the acute phase.<sup>1</sup>

In conclusion, post dengue infectious should be considered in patients with incapacitating symptoms for several months after resolution of acute phase of dengue fever. Unnecessary tests should be avoided in the absence of other indicators. This is a rare condition and is generally treated symptomatically. However, it can result in significantly reduced functional status as in our patient who was otherwise healthy and well built.

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## Instructions to Authors

### Scope

The Infectious Diseases Society of Pakistan sponsors the Infectious Disease Journal of Pakistan (IDJ). The Journal accepts Original Articles, Review Articles, Brief Reports, Case Reports, Short Communications, Letter to the Editor and Notes and News in the fields of microbiology, infectious diseases, public health; with laboratory, clinical, or epidemiological aspects.

### Criteria for publication

All articles are peer reviewed by the IDSP panel of reviewers. After that the article is submitted to the Editorial Board. Authors may submit names and contact information of 2 persons who potentially could serve as unbiased and expert reviewers for their manuscript, but IDSP reserves the right of final selection.

### Submission of the Manuscript

Manuscripts must be formatted according to submission guidelines given below, which are in accordance with the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals" (originally published in *N Engl J Med* 1997;336:309-15). The complete document appears at [www.icmje.org](http://www.icmje.org). Please submit one complete copy of the manuscript and all enclosures to **The Managing Editors, Infectious Diseases Journal of Pakistan, Department of Pediatrics & Child Health, The Aga Khan University, Stadium Road, P.O. Box 3500, Karachi 74800, Pakistan**. An electronic copy of the manuscript must also be sent to [pak\\_idj@yahoo.com](mailto:pak_idj@yahoo.com). All manuscripts submitted to IDJP must be accompanied by an Authorship Declaration stating that '*The authors confirm that the manuscript, the title of which is given, is original and has not been submitted elsewhere. Each author acknowledges that he/she has contributed in a substantial way to the work described in the manuscript and its preparation*'. Upon submission a manuscript number will be assigned which should be used for all correspondence.

### Manuscript Categories

#### I. Original Articles

Articles should report original work in the fields of microbiology, infectious disease or public health. The word limit for original articles is 2000.

#### Title page

This should list the (i) title of the article, (ii) the full names of each author with highest academic degree(s), institutional addresses and email addresses of all authors. (iii) The corresponding author should also be indicated with his/her name, address, telephone, fax number and e-mail address. (iv) A short running title of not more than 40 characters (count letters and spaces) placed at the foot end of the title page. (v) a conflict of interest statement should also be included in this section.

### Abstract

Abstract should not exceed 250 words and must be structured in to separate sections headed *Background, Methods, Results and Conclusions*.

Please do not use abbreviations or cite references in the abstract. A short list of four to five key words should be provided to facilitate.

### Background

The section must clearly state the background to the research and its aims. Controversies in the field should be mentioned. The key aspects of the literature should be reviewed focusing on why the study was necessary and what additional contribution will it make to the already existing knowledge in that field of study. The section should end with a very brief statement of the aims of the article.

### Materials and Methods

Please provide details of subject selection (patients or experimental animals). Details must be sufficient to allow other workers to reproduce the results. The design of study and details of interventions used must be clearly described. Identify precisely all drugs and chemicals used, including generic name(s) and route(s) of administration. All research carried out on humans must be in compliance with the *Helsinki Declaration*, and animal studies must follow internationally recognized guidelines. The authors are expected to include a statement to this effect in the Methods section of the manuscript. A description of the sample size calculation and statistical analysis used should be provided.

### Results

Present results in logical sequences in the text, tables and illustrations. Articles can have a maximum of 5 illustrations (in a combination of figures and tables) per article. The results should be in past tense and repetition of results presented in the tables should be avoided. Exact *P*-values should be reported along with reporting of OR and RR with their Confidence Intervals where applicable.

### Discussion

Emphasize the new and important aspects of the study and conclusions that follow from them. Do not repeat the details from the results section. Discuss the implications of the findings and the strengths and limitations of the study. Link the conclusions with the goals of the study but avoid unqualified statements and conclusion not completely supported by your data.

### Acknowledgments

Acknowledge any sources of support, in the form of grants, equipment or technical assistance. The source of funding (if any) for the study should be stated in this section. Please see below for format of **References, Figures and Tables**.

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## II. Review Articles

Authoritative and state of the art review articles on topical issues are also published, with a word limit of 2000. It should consist of critical overview of existing literature along with reference to new developments in that field. These should be comprehensive and fully referenced. Articles should contain an Abstract; Main Text divided into sections, Conclusions and References.

## III. Brief Reports

Short clinical and laboratory observations are included as Brief Reports. The text should contain no more than 1000 words, two illustrations or tables and up to 10 references.

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Instructive cases with a message are published as case reports. Routine syndromes or rare entities without unusual or new features are invariably rejected. The text should contain no more than 1000 words, two illustrations or tables and up to 10 references. The authorship should not exceed 3-4 persons.

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These may relate to material published in the IDJP, topic of interest pertaining to infectious diseases, and/or unusual clinical observations. A letter should not be more than 300 words, one figure and 3-5 references.

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Informative, breaking news updates in infectious diseases from around the world (approx. 200 words).

## VII. Notices

Announcements of conferences, symposia or meetings may be sent for publication at least 12 weeks in advance of the meeting date. Details of programs should not be included.

## References

Number references consecutively in the order in which they are first mentioned in the text. Identify references in text, tables and legends by Arabic numerals (in superscript). References cited only in tables or in legends to figures should be numbered in accordance with a sequence established by the first identification of the particular table or illustration. Bibliography should be given in order. Authors, complete title, journal name (Abbr), year, vol, issue, page numbers. According to "Uniform

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## Tables and Figures

Data reported either in a table or in a figure should be illustrative of information reported in the text, but should not be redundant with the text. Each table must be presented on a separate sheet of paper and numbered in order of appearance in the text. Table should be numbered consecutively in Arabic numerals. Tables and Figures legends should be self-explanatory with adequate headings and footnotes. Results which can be described as short statements within the text should not be presented as figures or tables.

## Illustrations

Illustrations should be numbered, given suitable legends and marked lightly on the back with the author's name and the top edge indicated. Original drawings may be submitted although high quality glossy photographs are preferable. They should be kept separate from the text. If possible, figures should be submitted in electronic format as either a TIFF (tagged image file format) or JPEG format. Minimum resolution for scanned artwork is:

- √ Black & white line illustration (e.g. graphs): 600 dpi
- √ Black & white halftone illustrations (e.g. photographs): 300 dpi
- √ Color illustrations: 400 dpi (note that color images should be split CMYK not RGB)

## Plagiarism

Authors should refrain from plagiarism and should double check their work before submitting it for publication. Adequate references should be provided for text from other sources.

## Authorship criteria

Those who have contributed sufficiently to the conceptualization, design, collection and analysis of data and writing of the manuscript should be granted authorship. Ideally all authors should be from the same department except for studies that are multi center or multispecialty.

## Instructions updated - April 2012.

## Editor IDJ

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